Anesthesiology
81:289–298, 1994

J. B. Lippincott Company, Philadelphia

Epidural Anesthesia Increases Apparent Leg Temperature and Decreases the Shivering Threshold

Thomas H. Emerick, M.D., Makoto Ozaki, M.D.,* Daniel I. Sessler, M.D.,†*
Kristin Walters, B.A.,‡ Marc Schroeder, B.A.‡

Background: **Lower core temperatures than usual are required to trigger shivering during epidural and spinal anesthesia, but the etiology of this impairment remains unknown. In this investigation, we propose and test a specific mechanism by which a peripheral action of regional anesthesia might alter centrally mediated thermoregulatory responses. Conduction anesthesia blocks all thermal sensations; however, cold signals are disproportionately affected because at typical leg temperatures mostly cold receptors fire tonically. It thus seems likely that epidural and spinal anesthesia increase the leg temperature perceived by the thermoregulatory system. Because skin temperature reportedly contributes 5–20% to thermoregulatory control, increased apparent (as distinguished from actual) leg temperature would produce a complimentary decrease in the core temperature triggering thermoregulatory shivering. Accordingly, we tested the hypothesis that abnormal tolerance for hypothermia during epidural anesthesia coincides with an increase in apparent leg temperature. We defined apparent temperature as the leg-skin temperature required to induce a reduction in the shivering threshold comparable to that produced by epidural anesthesia.**

Methods: **Six women were studied on 4 randomly ordered days: (1) leg-skin temperature near 32°C; (2) leg-skin temperature near 36°C; (3) leg-skin temperature near 38°C; and (4) epidural anesthesia without leg-warming (leg-skin temperature ≈ 34°C). At each designated leg temperature, core hypothermia sufficient to evoke shivering was induced by central venous infusion of cold fluid. Upper-body skin temperature was kept constant throughout. In each volunteer, linear regression was used to calculate the correlation between the shivering thresholds on the 3 nonepidural days and concurrent leg temperatures. The slope of these regression equations thus indicated the extent to which leg-warming increased thermoregulatory tolerance for core hypothermia, and was expressed as a percentage leg-skin and leg-tissue contribution to total thermal afferent input. The skin and tissue temperatures that would have been required to produce the observed shivering threshold during epidural anesthesia, the apparent temperatures, were then interpolated from the regression.**

Results: **There was a good linear relation between the shivering threshold and leg-skin temperature (r^2 = 0.94 ± 0.06). The contribution of leg-skin temperature to the shivering threshold was 11 ± 3% of the total thermal input. Apparent leg-skin temperature during epidural anesthesia was 37.8 ± 0.5°C, which exceeded actual leg-skin temperature by ≈ 4°C. The contribution of leg-tissue temperature to the shivering threshold was 19 ± 7% of the total. Apparent leg-tissue temperature during epidural anesthesia was 37.1 ± 0.4°C, which exceeded actual leg-skin temperature by ≈ 2°C.**

Conclusions: **Because leg-skin contributed ≈ 11% to the shivering threshold, it is unlikely that the entire skin surface contributes at much less than 20%. These data suggest that the shivering threshold during epidural anesthesia is reduced by a specific mechanism, namely that conduction block significantly increases apparent (as distinguished from actual) leg temperature. (Key words: Anesthesia: epidural. Temperature, regulation: setpoint; shivering; threshold. Thermoregulation.)**

This article is accompanied by an editorial. Please see: Giesbrecht GG: Human thermoregulatory inhibition by regional anesthesia. ANESTHESIOLOGY 81:277–281, 1994.

THE normal responses of regulatory control systems to thermal perturbations have been well described.[1] Similarly, the pattern of alteration during general anesthesia is well known,[2] and the patterns during spinal[3] and epidural[4,5] anesthesia have been described at least partially. The mechanisms, however, by which general and regional anesthesia impair thermoregulatory control remain unknown. Current understanding of anesthetic-induced thermoregulatory impairment thus remains largely empirical. As a result, our ability to predict thermoregulatory responses to novel anesthetic situations remains limited. In this study we propose and evaluate a specific mechanism by which peripheral

* Research Fellow.

† Associate Professor.

‡ Staff Research Associate.

Received from the Thermoregulation Research Laboratory, Department of Anesthesia, University of California, San Francisco, California. Accepted for publication January 25, 1994. Supported by Augustine Medical, the Joseph Drown Foundation, and National Institutes of Health grants GM39723 and GM49670. M.O. was the 1992–1993 Augustine Scholar.

Address correspondence to Dr. Sessler: Department of Anesthesia, C-214, University of California, San Francisco, School of Medicine, Third and Parnassus Avenue, San Francisco, California 94143-0648.

nerve block might alter centrally mediated thermoregulatory control. This study is the first to test a specific mechanism by which anesthesia impairs centrally mediated thermoregulatory control.

Hypothermia during regional anesthesia is as common, and nearly as severe, as that occurring during general anesthesia.[6,7] Comparable thermal lability occurs in patients with spinal cord transections, causing major problems in some cases.[8] Hypothermia results, in part, because lower core temperatures than usual are required to trigger shivering during major conduction anesthesia.[9] Typically, the shivering threshold (core temperature triggering shivering) is reduced $\approx$ 0.6°C by spinal anesthesia,[3] but the etiology of this impairment remains unknown. Although small compared with the inhibition produced by general anesthetics,[10–12] 0.6°C far exceeds the normal sweating-to-vasoconstriction interthreshold range of $\approx$ 0.2°C.[13]

Induction of regional anesthesia usually is accompanied by a sensation of increased warmth in the affected body parts; patients, for example, often comment that their legs feel warmer after induction of epidural or spinal anesthesia. Some of this warming sensation certainly is a response to an actual increase in leg temperature, resulting from a core-to-peripheral redistribution of body heat.[5] However, the $\approx$ 1°C actual increase in leg-skin temperature[4,5] may not fully explain the reported sensation of warmth. Furthermore, the sensation of relative warmth persists when surgical levels of anesthesia are established—and thus well after actual leg temperature can be directly sensed.[4]

Conduction anesthesia blocks all thermal sensations; however, cold signals are disproportionately affected because at typical skin temperatures mostly cold receptors fire tonically.[14,15] It thus seems likely that epidural and spinal anesthesia increase the leg temperature perceived by the thermoregulatory system. Because skin temperature reportedly contributes 5–20% to thermoregulatory control,[16–18] increased apparent (as distinguished from actual) leg temperature would produce a complimentary decrease in the core temperature triggering thermoregulatory shivering.

Accordingly, we tested the hypothesis that abnormal tolerance for hypothermia during epidural anesthesia coincides with an increase in apparent leg temperature. The apparent temperature was inferred from the actual leg temperature required to induce a reduction in the shivering threshold comparable to that observed during epidural anesthesia. In the process of determining apparent leg temperature, we were able for the first time to calculate the extent to which leg temperature contributes to total thermal afferent information under steady state conditions.

It is likely that thermal receptors exist in human muscle, but their physiologic importance (if any) has yet to be elucidated. Consequently, the independent contributions of leg-skin and leg-tissue temperatures to thermoregulatory responses remains unknown. Apparent temperatures therefore were calculated independently with both leg-skin and leg-tissue temperatures.

Materials and Methods

With approval from the Committee on Human Research at the University of California, San Francisco and informed consent, we studied six female volunteers. None was obese, was taking medication other than oral contraceptives, or had a history of thyroid disease, dysautonomia, Raynaud's syndrome, or malignant hyperthermia. Four volunteers used oral contraceptives and were studied during weeks 1 and 2 of their 3-week-on/1-week-off contraceptive cycle; the remaining volunteers were studied during the first 10 days of their menstrual cycles.

The volunteers' height was 164 ± 6 cm (mean ± SD), weight 56 ± 8 kg, and age 25 ± 2 yr. The percentage of body fat was 21 ± 4, as determined by infrared interactance[19] (Futrex 1000, Futrex, Hagerstown, MD).

Volunteers were studied on 4 randomly ordered days: (1) leg-skin temperature near 32°C (cold); (2) leg-skin temperature near 36°C (warm); 3) leg-skin temperature near 38°C (hot); and (4) epidural anesthesia without leg-warming (epidural). At each designated leg-skin temperature, core hypothermia sufficient to evoke shivering was induced by central venous infusion of cold lactated Ringer's solution. Throughout the 4 study days, upper-body skin temperature was kept constant.

Protocol

Judging from preliminary data, we expected the threshold differences produced by leg-skin temperature manipulations ($\approx$ 0.7°C) to be small compared with circadian core temperature changes ($\approx$ 1°C).[20] Consequently, each subject was scheduled such that shivering occurred at nearly the same time on each of the 4 study days. The volunteers fasted for 8 h before arriving at the laboratory; during studies, they were min-

imally clothed and rested supine on a standard operating room table. Ambient temperature was maintained at 21.9 ± 0.8°C and ambient relative humidity at 40 ± 4% during the study period (humidity and temperature transmitter model HX93, Omega Engineering, Stamford, CT).

After standard anesthetic safety monitors were positioned, a 16-G catheter, to be used for subsequent infusion of cold fluid, was inserted into the superior vena cava *via* the right internal jugular vein. A 14-French Foley catheter was inserted into the bladder. On the epidural day, a catheter was inserted into the epidural space *via* the L3–L4 interspace. Throughout the 4 study days, upper-body skin temperature was kept constant, near 35.7°C, by manipulating output of a Bair Hugger forced-air warmer[21] (cover model 420 and blower model 200, Augustine Medical, Eden Prairie, MN) modified to allow incremental temperature control by a rheostat. In preliminary studies we found results inconsistent unless upper body skin temperatures were carefully controlled. We thus actively maintained skin temperature within several 10ths of 1°C of our target temperature throughout each trial.

On the cold day, the legs were exposed to the ambient environment. On the warm day, a pediatric-sized circulating-water mattress (Blanketrol II and Maxi-Therm blanket, Cincinnati Sub-Zero, Cincinnati, OH) positioned under the legs was set to 37°C and a lower-body forced-air cover was positioned above the legs, with the Bair Hugger blower set to "low" (≈ 37°C). Similarly, hot legs were produced by increasing temperature of the water mattress to 42°C and setting the forced-air blower to "high" (≈ 42°C); to further augment skin and tissue temperature on this day, the legs were covered with plastic film that prevented cutaneous evaporative heat loss.

Induction of epidural anesthesia was preceded by 1 h of cutaneous prewarming to minimize redistribution hypothermia.[22] Warming was continued during the first 30 min of anesthetic administration, then the legs were exposed to the ambient environment for the duration of the protocol. These 30 min of warming after induction of anesthesia were sufficient to return core temperature to control values. During induction of epidural anesthesia, ≈ 1,000 ml warmed lactated Ringer's solution was administered intravenously to minimize sympathectomy-induced vascular volume shifts.

The epidural catheter was injected with 3 ml 2% 2-chloroprocaine (Chloroprocaine HCl, *United States Pharmacopeia*, Abbott Laboratories, North Chicago, IL) with epinephrine 1:100,000. This test dose was followed in 5 min by slow administration of 15–20 ml 2% 2-chloroprocaine without epinephrine. The initial volume of 2-chloroprocaine was chosen based on each volunteer's height and calculated to produce a dermatomal level of sensory blockade near T10, as determined by loss of cutaneous cold sensation and response to pinprick. Subsequently, a continuous infusion of 2% 2-chloroprocaine was administered at a rate of 13–18 ml/h to maintain a comparable sensory blockade level. In preliminary studies, we noticed that apparent temperatures were less in volunteers with constricted toes than those with dilated toes (although cold sensation was blocked in each case). Consequently, the epidural catheter position was adjusted if necessary and additional anesthetic administered to maintain toe vasodilation in each volunteer throughout anesthesia. Chloroprocaine was chosen as the epidural anesthetic because it is rapidly metabolized in plasma; central recirculation of this anesthetic *via* blood thus is unlikely to alter thermoregulatory responses.

As previously described,[23] core hypothermia was induced by central-venous infusion of lactated Ringer's solution cooled to ≈ 3°C with an aluminum cardiopulmonary bypass heat exchanger immersed in an ice-water slurry. Cooling was begun after 1.5 h of leg exposure to ambient temperature on the cold day and 2.5 h of leg heating on the warm and hot days. Core cooling on the epidural day was initiated ≈ 1 h after induction of epidural anesthesia. These times were chosen to produce relatively homogeneous leg-tissue temperatures under each condition. Cold fluid was administered at a rate sufficient to decrease core temperature ≈ 0.8°C/h, and was continued until initiation of shivering.

Monitoring

Core temperature was measured at the tympanic membrane with Mon-a-Therm thermocouples (Mallinckrodt Anesthesia Products, St. Louis, MO). Visual inspection with an otoscope confirmed that the ear canal was free of wax in each volunteer. The aural probe then was inserted by volunteers until they felt the thermocouple touch the tympanic membrane; appropriate placement was confirmed when volunteers easily detected a gentle rubbing of the attached wire. The aural canal was occluded with cotton, the probe securely taped in place, and a gauze bandage positioned over the external ear.

Upper-body skin-surface temperatures were computed from measurements at seven sites by assigning the following regional percentages to each area: head 11%, upper arms 17%, forearms 11%, hands 5%, fingers 4%, back 34%, and chest 18%. Leg-skin surface temperatures similarly were derived from seven sites: medial thigh 17%, lateral thigh 17%, posterior thigh 19%, anterior calves 20%, posterior calves 11%, feet 11%, and toes 5%.[24]

The length of the thigh (iliac crest to midpatella) and lower leg (midpatella to sole of foot) were measured in cm. Similarly, circumference was measured at the midpoint of the thigh and mid upper calf (one quarter of the distance from the patella to the sole of the foot) and midlower calf (three quarters of the distance from the patella to the foot). Right leg muscle temperatures were recorded with disposable 8-, 18-, and 38-mm 21-G needle thermocouples (Mallinckrodt Anesthesiology Products) inserted perpendicular to the skin surface. After intradermal injection of $\approx$ 0.1 ml of 1% lidocaine, one needle of each length was inserted several cm lateral to the anterior midline of the thigh. Needles similarly were inserted into the mid upper calf and mid lower calf. In each case, needles were inserted at the same place in which leg segment circumference was measured. Skin-surface temperatures were recorded immediately adjacent to each set of needles, and directly posterior to each set.

Calf minus toe, skin-surface temperature gradients were used as an index of leg perfusion.[10] As in previous studies,[25] we considered a gradient exceeding 4°C to indicate vasoconstriction, and a gradient less than 0°C to indicate vasodilation. Core, skin-surface, and muscle temperatures were recorded from thermocouples connected to two calibrated Iso-Thermex 16-channel electronic thermometers having an accuracy of 0.1°C and a precision of 0.01°C (Columbus Instruments International, Columbus, OH). Individual temperatures and appropriate averages were displayed at 1-s intervals.

Oxygen consumption was measured with a canopy-based metabolic monitor (Deltatrac, SensorMedics, Yorba Linda, CA). Measurements were averaged over 1-min intervals and recorded every five min. A sudden and sustained increase in oxygen consumption (generally exceeding 150% of baseline values) identified shivering. The time at which significant shivering was initiated was subsequently determined, from a plot of oxygen consumption *versus* time, by an investigator blinded to the specific trial and core temperature. The core temperature triggering shivering defined the threshold for this response.

Heart rate was monitored continuously by three-lead electrocardiography. Oxyhemoglobin saturation was measured continuously by pulse oximetry, and blood pressure was determined oscillometrically at 5-min intervals at the left upper arm with the Modulus CD Anesthesia System (Ohmeda, Madison, WI). Analog and serial thermoregulatory data were recorded at 5-min intervals using a modification of a previously described data-acquisition system.[23] Anesthetic data were recorded with IdaCare version 1.3 (Hermes Systems, Belgium), which is Macintosh (Apple, Cupertino, CA)–based patient information management software. Both systems operated asynchronously on a Macintosh FX computer.

Leg-tissue Temperature

The leg was divided into three segments: thigh, upper calf, and lower calf–foot. Each segment was further divided into an anterior and posterior section, with one third of the estimated mass considered to be posterior.

Anterior segment tissue temperatures, as a function of radial distance from the center of the leg segment, were calculated from skin-surface temperatures and muscle temperatures (8, 18, and 38 mm below the surface) by parabolic regression.§ Temperature at the center of the thigh was set to core temperature. In contrast, temperature at the center of the lower leg segments was estimated from the regression equation with no similar assumption. This regression assumes segmental tissue temperature is radially symmetrical. Results of the parabolic regression were expressed by the equation

$$T(r) = a_0 + a_2 r^2, \quad (1)$$

where T(r) = temperature (degrees Celsius) at radius r (centimeters); a_0 (degrees Celsius) = temperature at the center of the leg segment; and a_2 (degrees Celsius per squared centimeter) = a regression constant. The average temperature of the leg segments (T_{Ave}) was determined by integrating equation 1 from 0 to r:

$$T_{Ave} = a_0 + \frac{a_2 r^2}{2}. \quad (2)$$

§ Regression constants were determined by reflecting temperatures around the enterline and fitting the values to a second-order polynomial least-squares regression. With this technique, the coefficient of the linear term is zero, leaving a parabolic equation.

We previously have described the derivation of these formulas and their limitations.[25]

We did not measure posterior leg-tissue temperatures. Rather than assume full radial symmetry, we assumed only that radial temperature distribution in the posterior leg segments would also be parabolic. Accordingly, we calculated the regression constant a_2 in the posterior leg segments from equation 1, from a_0 determined from the adjacent anterior segment and the posterior segment skin temperature. Average posterior segment tissue temperature then was determined by inserting these values into equation 2.

Average temperatures for the entire leg were calculated by weighting the values from each of the six segments in proportion to their estimated masses. The right and left legs were treated comparably throughout this study, so we assumed that average tissue temperatures in the two legs were similar.

Statistical Analysis

In each volunteer, linear regression was used to calculate the correlation between the shivering thresholds on the 3 nonepidural days and concurrent leg-skin temperatures. That is, a linear equation was derived from the three sets of shivering thresholds and respective leg-tissue temperatures on the nonepidural days:

$$T_{Core} = ST_{Skin} + K, \quad (3)$$

where T_{Core} = core temperature in degrees Celsius; S = slope; T_{Skin} = leg-skin temperature (degrees Celsius); and K = a constant.

The slope S of this regression equation thus indicated the extent to which leg-warming increased thermoregulatory tolerance for core hypothermia without anesthesia (*i.e.*, how much leg-warming was required to reduce the shivering threshold). To determine the fractional contribution of leg-skin to thermoregulatory control of shivering, we assumed the following relation:

$$T_{MBT} = \beta T_{Skin} + (1 - \beta)T_{Core}, \quad (4)$$

where T_{MBT} = the shivering threshold in terms of mean body temperature and β = the cutaneous contribution to the threshold. Rearranging this equation yields

$$T_{Core} = \left(\frac{-\beta}{1 - \beta}\right)T_{Skin} + \frac{T_{MBT}}{1 - \beta}. \quad (5)$$

Combining equations 3 and 5, it is apparent that

$$S = \frac{-\beta}{1 - \beta}, \quad (6)$$

and consequently that

$$\beta = \frac{S}{S - 1}. \quad (7)$$

The skin temperature that would have been required to produce the observed shivering threshold during epidural anesthesia then was interpolated from the regression; we designated this value as the apparent skin temperature. A graphic example of this process is shown in figure 1; in practice, the apparent temperature was calculated by solving the linear regression equation for leg-skin temperature after inserting the observed shivering threshold during epidural anesthesia.

A similar regression between the shivering thresholds and average leg-tissue temperatures was computed in each volunteer. The contribution of leg-tissue to control of shivering was again calculated from the slope by equation 7. A value designated the apparent tissue temperature was interpolated from this regression equation by inserting the shivering threshold during epidural anesthesia.

Skin and tissue temperatures, and the rates of core cooling during the 4 study days were compared by one-way analysis of variance and Scheffé's F tests. The regression coefficients, the apparent temperatures, and differences between the apparent temperatures and the actual leg temperatures during epidural anesthesia and those on the cold day were compared by unpaired, two-tailed *t* tests. Results are expressed as means ± standard deviations; differences were considered statistically significant when $P < 0.01$.

Results

Epidural-induced sensory block level at the time of the shivering threshold averaged T10 ± 1, and ranged from T9 to T11. The legs were vasodilated (calf minus toe, skin-temperature gradient < 0°C) before induction of epidural anesthesia in all volunteers. The toes remained dilated throughout anesthesia, indicating that sympathetic efferent nerves supplying the legs were blocked.

Upper-body skin temperatures were well controlled, with no statistically significant or clinically important differences among the volunteers or on the different study days in individual volunteers. As intended, leg-skin and leg-tissue temperatures differed markedly on the 3 nonepidural days. One volunteer refused the

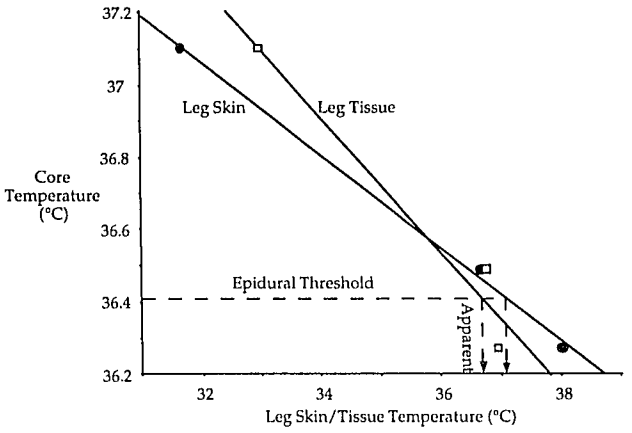

Fig. 1. Results in one volunteer. There was a good linear relation (solid lines) between core temperature (T_{Core}) and leg-skin temperature (T_{Skin}) at the shivering thresholds ($r^2 = 0.99$) (filled circles). Similarly, there was a good correlation between core temperature and average leg-tissue temperature (T_{Tissue}) at the shivering thresholds ($r^2 = 0.95$) (open squares). Increasing leg-skin temperature reduced the shivering threshold, but comparably increasing leg-tissue temperature reduced it even more. The regression equation for core temperature in terms of leg-skin temperature was $T_{Core} = (-0.13)T_{Skin} + 41.2$; in this example, the slope = −0.13. The extent to which leg-skin temperature contributed to central thermoregulatory control of shivering (β) was calculated from the slope (S) of the regression of leg-skin temperature *versus* core temperature, with the formula $\beta = S/(S - 1)$. In this example, leg-skin contributed 11% of the total thermal input. The regression equation for leg tissue was $T_{Core} = (-0.18)T_{Tissue} + 43.0$; in this example, S = −0.18. The extent to which leg-tissue temperature contributed to central thermoregulatory control of shivering was again calculated from the slope, as above. In this example, leg tissue contributed 15% of the total thermal input. Apparent temperatures during epidural anesthesia were interpolated from the regressions of leg-skin and leg-tissue temperatures against the shivering threshold (dashed lines). That is, the shivering threshold during epidural anesthesia was inserted into the regressions and the corresponding leg-skin and leg-tissue temperatures calculated. Graphically, this calculation consists of extending a line from the shivering threshold (left axis) to the regression equations and then dropping perpendicular lines to the horizontal axis. The intersection of these perpendicular lines with the horizontal axis indicate the apparent leg-skin/tissue temperatures. The apparent temperature calculated from leg-skin temperature (37.1°C) exceeded that calculated from leg-tissue temperature (36.7°C). Actual leg-skin temperature at the shivering threshold during epidural anesthesia was 34.2°C; the corresponding leg-tissue temperature was 35.1°C. Both apparent temperatures substantially exceeded leg temperatures on the cold day (typical clinical situation) and actual leg temperatures during epidural anesthesia.

needle thermocouples on 2 of the study days. Consequently, we report leg-tissue temperatures and results derived from those values only in five volunteers. Core cooling rates during central venous administration of cold lactated Ringer's solution were similar on the 4 study days (table 1).

The shivering threshold during epidural anesthesia was 0.7 ± 0.2°C less than that on the cold study day. There was a good linear relation between the shivering threshold and leg-skin and average leg-tissue temperatures. The correlation coefficients (r^2) averaged ≈ 0.9, and in all cases exceeded 0.8. The contribution of leg-skin temperature to the shivering threshold was 11 ± 3% of the core contribution. The contribution of leg-tissue temperature to the shivering threshold was 19 ± 7% of the core contribution.

In all cases, the shivering threshold during epidural anesthesia was between those recorded on the warm and hot days. Consequently, it was not necessary to extrapolate beyond our data when interpolating apparent temperatures from the regressions of leg-skin or tissue temperatures. Apparent temperatures were similar when calculated from leg-skin (37.8 ± 0.5°C) and leg-tissue (37.1 ± 0.4°C) temperature. Apparent skin and apparent tissue temperatures significantly exceeded actual leg-skin and leg-tissue temperatures at the shivering threshold, both during epidural anesthesia and on the cold study day (table 2). As an example, the results in one volunteer are shown in figure 1.

Discussion

Regional anesthesia may interfere with all components of thermoregulation: afferent sensing, central control, and efferent responses.[26,27] Efferent thermoregulatory responses such as sweating, vasoconstriction, and shivering are clinically important responses[5,25,28,29] that are obliterated in areas blocked by regional anesthesia. However, there is considerable

Table 1. Skin and Tissue Temperatures, and Core Cooling Rates

	Cold	Warm	Hot	Epidural
Upper skin (°C)	35.5 ± 0.1	35.5 ± 0.1	35.5 ± 0.1	35.5 ± 0.1
Leg skin (°C)	32.0 ± 0.8	36.4 ± 0.7	38.2 ± 0.3	33.7 ± 0.5
Leg tissue (°C)	34.0 ± 0.8	36.4 ± 0.4	37.1 ± 0.4	34.7 ± 0.4
Cooling rate (°C/h)	0.7 ± 0.2	0.8 ± 0.1	0.8 ± 0.1	0.9 ± 0.2

Values are given for upper body skin temperatures, leg skin temperatures, average leg tissue temperatures, and core cooling rates at the shivering threshold on each of the four study days. There were no statistically significant or clinically important differences in upper body skin temperatures or core cooling rates on the different study days. By design, leg skin and leg tissue temperatures differed significantly on each of the three nonepidural days.

evidence that responses above the level of anesthetic-induced sympathetic and motor block also are altered. In 1972, Roe and Cohn[9] observed that 1–3°C hypothermia was typical during spinal anesthesia, perceptively postulating that it resulted because the shivering threshold was ≈ 1°C below normal. Although central thermoregulatory responses in that study may have been depressed by concomitant use of sedative and analgesic adjuvants,[30] we have demonstrated similar abnormal tolerance to core hypothermia during epidural anesthesia in nonsedated patients[31] and volunteers.[4]

It is unlikely that anesthetics injected intrathecally or extradurally diffuse rostrally in amounts sufficient to directly anesthetize higher regulatory centers. An alternative explanation is that epidurally administered anesthetics might indirectly impair central thermoregulation *via* absorption of local anesthetic into the blood stream and subsequent recirculation to the central nervous system. However, plasma lidocaine concentrations similar to those observed during epidural anesthesia do not alter the vasoconstriction or shivering thresholds.[32] Furthermore, chloroprocaine epidural anesthesia causes distinct thermoregulatory impairment,[5] although this drug is rapidly metabolized in plasma. These data, therefore, suggest that another mechanism mediates thermoregulatory impairment during regional anesthesia.

Both skin and core temperatures contribute to thermoregulation.[33–36] Most warm receptors are quiescent at typical skin temperatures (≈ 33°C).[14,15] Consequently, at typical ambient temperatures, predominantly cold signals converge on the central thermoregulatory system. Although regional anesthesia blocks all thermal information from the lower portion of the body, tonic cold signals would be the major traffic disrupted. In this scenario, the central thermoregulatory system might interpret the absence of tonic cold input as relative warming, and therefore an increase in apparent leg temperature.

An increase in apparent leg temperature, combined with intact central thermoregulatory processing, would alter responses to core hypothermia in the same fashion as leg-warming without anesthesia. Our data are consistent with this mechanism, and demonstrate that apparent leg-skin temperature far exceeds both actual leg temperatures during epidural anesthesia and leg temperature on the cold day (representing the typical clinical situation). Apparent leg-tissue temperature similarly exceeded both actual tissue temperature during epidural anesthesia and on the cold day. The associated reduction in the shivering threshold on the epidural *versus* cold study days was 0.7 ± 0.2°C, which is similar to values previously reported during epidural[4] and spinal[3] anesthesia.

Table 2. Correlation Coefficients, Apparent Temperatures, and the Difference between Apparent and Actual and Cold Leg Temperatures

	Skin	Tissue
Correlation (r^2)	0.94 ± 0.06	0.91 ± 0.08
Apparent (°C)	37.8 ± 0.5	37.1 ± 0.4
Apparent − actual (°C)	4.1 ± 1.0*	2.3 ± 0.6*†
Apparent − cold (°C)	5.8 ± 1.0*	3.1 ± 0.7*†

Values are given for the correlation coefficients (r^2), apparent temperatures, apparent temperatures minus the actual leg temperatures during epidural anesthesia, and apparent temperatures minus leg temperatures on the cold study day (the typical clinical situation). Actual leg skin and tissue temperatures are those recorded at the shivering threshold during epidural anesthesia. Apparent temperatures during epidural anesthesia were interpolated from the regressions of leg skin and tissue temperatures against the shivering threshold, *i.e.*, the shivering threshold during epidural anesthesia was inserted into the regressions and the corresponding leg skin/tissue temperatures determined.

* $P < 0.01$ between apparent and actual leg temperatures during epidural anesthesia and between apparent and leg temperatures on the cold study day.

† $P < 0.01$ between skin and tissue.

The clinical importance of increased apparent leg temperature during regional anesthesia is illustrated in a recent study. Huffnagle *et al.*[37] observed that patients in a cool environment (who already were shivering), stopped shivering after induction of spinal anesthesia even though anesthesia decreased core temperature ≈ 1°C. Although the authors speculate that shivering was blocked by a sympathectomy-induced increase in skin temperature, our results suggest that inhibition more likely resulted from increased apparent (as distinguished from actual) lower-body skin temperature.

Our data quantify the leg temperature required to produce thermoregulatory impairment comparable to that induced by regional anesthesia. These data suggest that a high apparent leg temperature is the mechanism of that impairment. However, they do not exclude other, perhaps less likely, causes of impairment including direct inhibition of thermal integration at the level of the lumbar spinal cord. Some integration does occur at that level,[38] although most thermoregulatory processing occurs at higher levels, including the brainstem, midbrain, and hypothalamus.[39–41]

A linear relation between skin and core temperatures triggering thermoregulation responses is consistent with previous studies[17,18] and our (unpublished) data in nonanesthetized volunteers. For practical reasons, we evaluated shivering thresholds without anesthesia

only at three different leg temperatures. Thus only three sets of data were included in our regression calculations. More data would increase the accuracy of the regression equations; nonetheless, the correlation coefficients were high and the relations clearly linear over the studied range.

Linear models usually include cutaneous contributions ranging from 5%[17] to ≈ 20%[18] of the core input. The exact cutaneous contribution, however, remains unclear because it has proven difficult to independently manipulate core and skin temperatures in humans. Because of experimental difficulties, most studies evaluate only the thresholds for sweating and active vasodilation. Certainly, the distinct contributions of leg-skin and average leg-tissue temperatures to shivering have not previously been established under steady-state conditions. Our data indicate that the shivering threshold is ≈ 11% determined by leg-skin temperature. This value is strikingly similar to the 13% contribution of leg-skin temperature to control of sweating observed by Downey *et al.*[42] in a single patient having a complete T6 spinal cord transection. Because the legs represent roughly half the body surface area[24] and the upper body is more sensitive to thermal stimuli,[43] these data do not seem consistent with a total cutaneous input much less than 20%.

The extent to which peripheral tissues other than skin contribute to thermoregulatory responses has not been extensively investigated. Although our data appear to suggest that both skin and tissue contribute, it is equally likely that leg-tissue changes were simply an artifact of synchronous skin- and tissue-warming. Far superior correlations (*i.e.*, higher r^2) between one of the leg temperatures and the corresponding shivering threshold would imply—but not prove—that that parameter best represented thermal input from the lower body. However, the correlations were comparable—and high. Consequently, we were unable to determine the physiologic significance of each independently. If, at some point, the contribution of leg tissue is determined (and differs from the skin contribution), the apparent tissue temperature reported here can be substituted for apparent skin temperature.

We have noticed in previous studies that pain resulting from a full bladder can alter thermoregulatory responses. To avoid this confounding factor, we drained urine *via* catheters in this study. Because bladder catheters are better tolerated by nonanesthetized women than men, we studied only women in this protocol. Thermoregulatory response thresholds generally are greater in women than in men[13,44,45] (although the increase may be due to normal morphometric differences[46–48]), and they consequently maintain higher core temperatures. Nonetheless, thermoregulatory impairment induced by regional anesthesia and changes in apparent leg temperature probably are similar in women and men. Pregnancy alters both normal thermoregulatory responses[49] and anesthetic action.[50,51] Very likely it also alters the thermoregulatory effects of anesthetics, but was not evaluated in this study.

The distal esophagus generally is considered the most reliable easily accessible core temperature monitoring site. Nonetheless, we measured core temperature at the tympanic membrane because many nonanesthetized subjects tolerate esophageal probes poorly. Under near steady-state conditions, as in this study, we[10,52] and others[53,54] have repeatedly found an excellent correlation between distal esophageal and tympanic membrane temperatures. We consequently expect that our results would be similar, and our conclusions comparable, had we measured core temperature in the distal esophagus.

We previously have described in detail the limitations of our average tissue temperature estimates.[25] Briefly, the technique assumes radial and longitudinal temperature symmetry within each leg segment, and a parabolic radial temperature distribution in the posterior segments. Although these assumptions surely are only approximately correct, it is unlikely that actual and estimated average leg-tissue temperatures differed substantially. At very least, estimates in these volunteers likely are better than those we have made previously because in this analysis we divided the leg into six segments, rather than just two.

In summary, this investigation proposed and tested a specific mechanism by which a peripheral action of regional anesthesia might alter centrally mediated thermoregulatory responses. Specifically, we evaluated the hypothesis that abnormal tolerance for hypothermia during epidural anesthesia coincides with an increase in apparent leg temperature. Epidural anesthesia decreased the shivering threshold 0.7 ± 0.2°C. This value is comparable to previously reported values, and far exceeds the normal interthreshold range (temperatures *not* triggering thermoregulatory responses). leg-skin temperature contributed 11 ± 3% to central control of shivering and leg-tissue temperature contributed 19 ± 7%. Apparent leg-skin and leg-tissue temperatures were similar: 37.8 ± 0.5°C and 37.1 ± 0.4°C, respectively.

Both values significantly exceeded actual leg temperatures during epidural anesthesia, and the values during the cold leg condition (the typical clinical condition). These data suggest that the shivering threshold is reduced during epidural anesthesia because anesthesia significantly increases apparent (as distinguished from actual) leg-skin and leg-tissue temperatures.

We thank Ohmeda for the loan of a Modulus CD integrated anesthesia machine; Mallinckrodt Anesthesiology Products for donation of the thermocouples we used; Hermes Systems for loan of an IdaCare automatic record-keeping system; and Cincinnati Sub-Zero for the loan of a Blanketrol II circulating-water warmer.

References

1. Simon E, Pierau F, Taylor DCM: Central and peripheral thermal control of effectors in homeothermic temperature regulation. Physiol Rev 66:235–300, 1986

2. Sessler DI: Perianesthetic thermoregulation and heat balance in humans. FASEB J 7:638–644, 1993

3. Kurz A, Sessler DI, Schroeder M, Kurz M: Thermoregulatory response thresholds during spinal anesthesia. Anesth Analg 77:721–726, 1993

4. Sessler DI, Ponte J: Shivering during epidural anesthesia. ANESTHESIOLOGY 72:816–821, 1990

5. Hynson J, Sessler DI, Glosten B, McGuire J: Thermal balance and tremor patterns during epidural anesthesia. ANESTHESIOLOGY 74: 680–690, 1991

6. Frank SM, Beattie C, Christopherson R, Norris EJ, Rock P, Parker S, Kimball AW: Epidural *versus* general anesthesia, ambient operating room temperature, and patient age as predictors of inadvertent hypothermia. ANESTHESIOLOGY 77:252–257, 1992

7. Hendolin H, Lansimies E: Skin and central temperatures during continuous epidural analgesia and general anaesthesia in patients subjected to open prostatectomy. Ann Clin Res 14:181–186, 1982

8. Hales JRS: Temperature regulatory set-point in paraplegics, Thermal Physiology. Edited by Attia M, Engel P. New York, Raven Press, 1984, pp 79–82

9. Roe CF, Cohn FL: The causes of hypothermia during spinal anesthesia. Surg Gynecol Obstetr 135:577–580, 1972

10. Støen R, Sessler DI: The thermoregulatory threshold is inversely proportional to isoflurane concentration. ANESTHESIOLOGY 72:822–827, 1990

11. Washington DE, Sessler DI, McGuire J, Hynson J, Schroeder M, Moayeri A: Painful stimulation minimally increases the thermoregulatory threshold for vasoconstriction during enflurane anesthesia in humans. ANESTHESIOLOGY 77:286–290, 1992

12. Hynson JM, Sessler DI, Belani K, Washington D, McGuire J, Merrifield B, Schroeder M, Moayeri A, Crankshaw D, Hudson S: Thermoregulatory vasoconstriction during propofol/nitrous oxide anesthesia in humans: Threshold and Sp_{O_2}. Anesth Analg 75:947–952, 1992

13. Lopez M, Sessler DI, Walter K, Emerick T, Ozaki M: Rate and gender-dependence of the sweating, vasoconstriction, and shivering thresholds in humans. ANESTHESIOLOGY 80:780–788, 1994

14. Pierau F, Wurster RD: Primary afferent input from cutaneous thermoreceptors. Fed Proc 40:2819–2824, 1981

15. Poulos DA: Central processing of cutaneous temperature information. Fed Proc 40:2825–2829, 1981

16. Benzinger TH, Pratt AW, Kitzinger C: The thermostatic control of human metabolic heat production. Proc Natl Acad Sci USA 47: 730–739, 1961

17. Wyss CR, Brengelmann GL, Johnson JM, Rowell LB, Silverstein D: Altered control of skin blood flow at high skin and core temperatures. J Appl Physiol 38:839–845, 1975

18. Tam H, Darling RC, Cheh H, Downey JA: The dead zone of thermoregulation in normal and paraplegic man. Can J Physiol Pharmacol 56:976–983, 1978

19. Conway JM, Norris KH, Bodwell CE: A new approach for the estimation of body composition: Infrared interactance. Am J Clin Nutr 40:1123–1130, 1984

20. Sessler DI, Lee KA, McGuire J: Isoflurane anesthesia and circadian temperature cycles. ANESTHESIOLOGY 75:985–989, 1991

21. Sessler DI, Moayeri A: Skin-surface warming: Heat flux and central temperature. ANESTHESIOLOGY 73:218–224, 1990

22. Glosten B, Hynson J, Sessler DI, McGuire J: Preanesthetic skin-surface warming reduces redistribution hypothermia caused by epidural block. Anesth Analg 77:488–493, 1993

23. Sessler DI, Moayeri A, Støen R, Glosten B, Hynson J, McGuire J: Thermoregulatory vasoconstriction decreases cutaneous heat loss. ANESTHESIOLOGY 73:656–660, 1990

24. Lund CC, Browder NC: The estimation of areas of burns. Surg Gynecol Obstet 79:352–358, 1944

25. Belani K, Sessler DI, Sessler AM, Schroeder M, McGuire J, Washington D, Moayeri A: Leg heat content continues to decrease during the core temperature plateau in humans. ANESTHESIOLOGY 78: 856–863, 1993

26. Hammel HT: Regulation of internal body temperature. Ann Rev Physiol 30:641–710, 1968

27. Hales JRS: Skin arteriovenous anastomoses: Their control and role in thermoregulation, Cardiovascular Shunts: Phylogenetic, Ontogenetic and Clinical Aspects. Edited by Johansen K, Burggren W. Copenhagen, Munksgaard, 1985, pp 433–451

28. Tankersley CG, Smolander J, Kenney WL, Fortney SM: Sweating and skin blood flow during exercise: Effects of age and maximal oxygen uptake. J Appl Physiol 71:236–242, 1991

29. Just B, Delva E, Camus Y, Lienhart A: Oxygen uptake during recovery following naloxone. ANESTHESIOLOGY 76:60–64, 1992

30. Kurz M, Belani K, Sessler DI, Kurz A, Larson M, Blanchard D, Schroeder M: Naloxone, meperidine, and shivering. ANESTHESIOLOGY 79:1193–1201, 1993

31. Glosten B, Sessler DI, Faure EAM, Støen R, Thisted RA, Karl L: Central temperature changes are not perceived during epidural anesthesia. ANESTHESIOLOGY 77:10–16, 1992

32. Glosten B, Sessler DI, Ostman LG, Faure EAM, Thisted RA: Intravenous lidocaine does not cause tremor or alter thermoregulation. Reg Anesth 16:218–222, 1991

33. Nagel A, Herold W, Roos U, Jessen C: Skin and core temperatures as determinants of heat production and heat loss in the goat. Pflügers Arch 406:600–607, 1986

34. Wenger CB, Roberts MF, Stolwijk JJA, Nadel ER: Forearm blood flow during body temperature transients produced by leg exercise. J Appl Physiol 38:58–63, 1975

35. Stolwijk JAJ, Hardy JD: Partitional calorimetric studies of responses of man to thermal transients. J Appl Physiol 21:967–977, 1966

36. Nadel ER, Cafarelli E, Roberts MF, Wenger CB: Circulatory regulation during exercise in different ambient temperatures. J Appl Physiol 46:430–437, 1979

37. Huffnagle HJ, Norris MC, Grieco WM, Leighton BL, Arkoosh VA, Huffnagle SL, Glosten B: Hypothermia and shivering during spinal anesthesia for cesarean delivery (abstract). ANESTHESIOLOGY 79:A1021, 1993

38. Simon E: Temperature regulation: The spinal cord as a site of extrahypothalamic thermoregulatory functions. Rev Physiol Biochem Pharmacol 71:1–76, 1974

39. Jessen C, Feistkorn G: Some characteristics of core temperature signals in the conscious goat. Am J Physiol 247:R456–R464, 1984

40. Jessen C, Mayer ET: Spinal cord and hypothalamus as core sensors of temperature in the conscious dog: I. Equivalence of responses. Pflügers Arch 324:189–204, 1971

41. Amini-Sereshki L, Zarrindast MR: Brain stem tonic inhibition of thermoregulation in the rat. Am J Physiol 247:R154–R159, 1984

42. Downey JA, Huckaba CE, Kelley PS, Tam HS, Darling RC, Cheh HY: Sweating responses to central and peripheral heating in spinal man. J Appl Physiol 40:701–706, 1976

43. Burke WEA, Mekjavic IB: Estimation of regional cutaneous cold sensitivity by analysis of the gasping response. J Appl Physiol 71:1933–1940, 1991

44. Washington D, Sessler DI, Moayeri A, Merrifield B, Prager M, McGuire J, Belani K, Hudson S, Schroeder M: Thermoregulatory responses to hyperthermia during isoflurane anesthesia in humans. J Appl Physiol 74:82–87, 1993

45. Avellini BA, Kamon E, Krajewski JT: Physiological responses of physically fit men and women to acclimation to humid heat. J Appl Physiol 49:254–261, 1980

46. Kolka MA, Stephenson LA, Rock PB, Gonzalez RR: Local sweating and cutaneous blood flow during exercise in hypobaric environments. J Appl Physiol 62:2224–2229, 1987

47. Stephenson LA, Kolka MA: Menstrual cycle phase and time of day alter reference signal controlling arm blood flow and sweating. Am J Physiol 249:R186–R191, 1985

48. Havenith G, van Midendorp H: The relative influence of physical fitness, acclimatization state, anthropometric measures and gender on individual reactions to heat stress. Eur J Appl Physiol 61:419–427, 1990

49. Hales JRS: Contribution of the uterus to circulatory requirements of exercise and heat stress in pregnant sheep, Thermal Physiology. Edited by Bell AW, Hales JRS, Fawcett AA, King RB. New York, Raven Press, 1984, pp 377–380

50. Strout CD, Nahrwold ML: Halothane requirement during pregnancy and lactation in rats. ANESTHESIOLOGY 55:322–323, 1981

51. Gintzler AR: Endorphin-mediated increases in pain threshold during pregnancy. Science 210:193–195, 1980

52. Lopez M, Ozaki M, Sessler DI, Valdes M: Mild core hyperthermia does not alter electroencephalographic responses during epidural/enflurane anesthesia in humans. J Clin Anesth 5:425–430, 1993

53. Cork RC, Vaughan RW, Humphrey LS: Precision and accuracy of intraoperative temperature monitoring. Anesth Analg 62:211–214, 1983

54. Shiraki K, Sagawa S, Tajima F, Yokota A, Hashimoto M, Brengelmann GL: Independence of brain and tympanic temperatures in an unanesthetized human. J Appl Physiol 65:482–486, 1988