Anesthesiology
80:268–277, 1994

Epidural Anesthesia Impairs Both Central and Peripheral Thermoregulatory Control during General Anesthesia

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Background: **The authors tested the hypotheses that: (1) the vasoconstriction threshold during combined epidural/general anesthesia is less than that during general anesthesia alone; and (2) after vasoconstriction, core cooling rates during combined epidural/general anesthesia are greater than those during general anesthesia alone. Vasoconstriction thresholds and heat balance were evaluated under controlled circumstances in volunteers, whereas the clinical importance of intraoperative thermoregulatory vasoconstriction was evaluated in patients.**

Methods: **Five volunteers were each evaluated twice. On one of the randomly ordered days, epidural anesthesia (≈T9 dermatomal level) was induced and maintained with 2-chloroprocaine. On both study days, general anesthesia was induced and maintained with isoflurane (0.7% end-tidal concentration), and core hypothermia was induced by surface cooling and continued for at least 1 h after fingertip vasoconstriction was observed. Patients undergoing colorectal surgery were randomly assigned to combined epidural/enflurane anesthesia (n = 13) or enflurane alone (n = 13). In appropriate patients, epidural anesthesia was maintained by an infusion of bupivacaine. The core temperature that triggered fingertip vasoconstriction identified the threshold.**

Results: **In the volunteers, the vasoconstriction threshold was 36.0 ± 0.2° C during isoflurane anesthesia alone, but significantly less, 35.1 ± 0.7° C, during combined epidural/isoflurane anesthesia. Cutaneous heat loss and the rates of core cooling were similar 30 min before vasoconstriction with and without epidural anesthesia. In the 30 min after vasoconstriction, heat loss decreased 33 ± 13 W when the volunteers were given isoflurane alone, but only 8 ± 16 W during combined epidural/isoflurane anesthesia. Similarly, the core cooling rates in the 30 min after vasoconstriction were significantly greater during combined epidural/isoflurane anesthesia (0.8 ± 0.2° C/h) than during isoflurane alone (0.2 ± 0.1° C/h). In the patients, end-tidal enflurane concentrations were slightly, but significantly, less in the patients given combined epidural/enflurane anesthesia (0.6 ± 0.2% *vs.* 0.8 ± 0.2%). Nonetheless, the vasoconstriction threshold was 34.5 ± 0.6° C in the epidural/enflurane group, which was significantly less than that in the other patients, 35.6 ± 0.8° C. When the study ended after 3 h of anesthesia, patients given combined epidural/enflurane anesthesia were 1.2° C more hypothermic than those given general anesthesia alone. The rate of core cooling during the last hour of the study was 0.4 ± 0.2° C/h during combined epidural/enflurane anesthesia, but only 0.1 ± 0.3° C/h during enflurane alone.**

Conclusions: **These data indicate that epidural anesthesia reduces the vasoconstriction threshold during general anesthesia. Furthermore, the markedly reduced rate of core cooling during general anesthesia alone illustrates the importance of leg vasoconstriction in maintaining core temperature. (Key words: Anesthesia, techniques: epidural; general. Anesthetics, volatile: enflurane; isoflurane. Measurement techniques, blood flow: plethysmography. Temperature, regulation: setpoint; threshold; vasoconstriction. Thermoregulation.)**

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Received from the Service d'Anesthesiologie, Centre Hospitalier Universitaire de Liege, Domaine Universitaire du Sart Tilman, Liege, Belgium; and the Thermoregulation Research Laboratory, University of California, San Francisco, California. Accepted for publication September 20, 1993. Supported by Augustine Medical and National Institutes of Health grants GM39723 and GM49670. Dr. Ozaki is the 1992–1993 Augustine Scholar. Presented in part at the annual meeting of the International Anesthesia Research Society, San Diego, California, March 20–23, 1993; and at the annual meeting of the American Society of Anesthesiologists, Washington, District of Columbia, October 8–14, 1993.

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AN internal redistribution of body heat usually decreases core temperature precipitously during the first

hour after induction of general anesthesia.[1] Subsequently, heat loss exceeding heat production gradually decreases core temperature.[2] Several hours after induction of general anesthesia, the progressive decrease in core temperature typically stops, identifying the core temperature plateau phase. This plateau can be a passive steady state (heat loss equaling metabolic heat production) in patients not becoming sufficiently cold to trigger thermoregulatory responses.[3] Alternatively, the plateau results when thermoregulatory vasoconstriction decreases cutaneous heat loss[4] and constrains metabolic heat to the core thermal compartment.[5]

Because the legs constitute nearly one half of the body surface area[6] and the bulk of the peripheral thermal compartment,[5] prevention of leg vasoconstriction by regional anesthesia may markedly impair regulatory ability to maintain core temperature in a cold environment. Consistent with such inhibition of peripheral vasoconstriction, core hypothermia is as common, and nearly as severe, during regional anesthesia as it is during general anesthesia.[7,8]

However, regional anesthesia not only directly prevents peripheral vasoconstriction, it also impairs central control of thermoregulatory responses. Specifically, the thresholds for both vasoconstriction and shivering (above the level of the block) are decreased during epidural[9] and spinal anesthesia.[10,11] Why regional anesthesia, which presumably has no direct central action, should impair central thermoregulatory control remains unclear. But if epidural anesthesia were to comparably impair central thermoregulatory control during general anesthesia, hypothermia might be particularly pronounced during combined regional/general anesthesia.

In this scenario, general anesthesia would inhibit centrally mediated vasoconstriction and shivering above the level of the regional block, while regional anesthesia would both centrally decrease the vasoconstriction threshold and directly prevent leg vasoconstriction. The result would be a reduced vasoconstriction threshold (compared with typical values during general anesthesia) and an absent plateau phase. Accordingly, we tested the hypotheses that: (1) the vasoconstriction threshold during combined epidural/general anesthesia is less than that during general anesthesia alone; and (2) after vasoconstriction, core cooling rates during combined epidural/general anesthesia are greater than those during general anesthesia alone.

We tested our hypotheses in two populations: young, healthy volunteers, and patients undergoing major abdominal surgery. We were able to precisely evaluate vasoconstriction thresholds and cutaneous heat loss in the volunteers, whereas the clinical importance of intraoperative thermoregulatory vasoconstriction was determined in the patients.

Materials and Methods

Both studies were conducted with approval of the local Ethics Committees. None of the subjects was obese, was taking medication likely to alter thermoregulatory or heat balance (*e.g.,* vasodilators, α-agonists, or β-blockers), or had a history of thyroid disease, dysautonomia, or Raynaud's syndrome.

Volunteers

We studied four men and one woman. The woman was studied during the first 10 days of her menstrual cycle. The volunteers' height was 171 ± 11 cm (mean ± SD), weight was 66 ± 12 kg, and age was 26 ± 4 yr. The volunteers each participated on two separate study days, randomly ordered. On one day, they were anesthetized with isoflurane alone, and on the other, they were given combined epidural/isoflurane anesthesia.

Protocol. Studies started at approximately 9:30 AM and volunteers fasted during the 8 h preceding each study. They were minimally clothed and reclined on their backs on a standard operating-room table. A pediatric-sized circulating water blanket set at 42° C (Blanketrol II, Maxi-Therm blanket #276; Cincinnati Sub-Zero, Cincinnati, OH) was positioned beneath their legs. Ambient temperature was maintained near 23° C throughout the studies. The percentage of body fat in the volunteers was 21 ± 7, as determined using infrared interactance (Futrex 1000; Futrex, Hagerstown, MD).[12]

On one of the study days, epidural anesthesia was induced without any preanesthetic medication. Using standard technique, a catheter was advanced 2–3 cm into the epidural space. The epidural catheter was then injected with 3 ml 2% 2-chloroprocaine (Chloroprocaine HCl, USP; Abbott Laboratories, 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. During induction of epidural anesthesia, 1,500 ml of lactated Ringer's solution warmed to 37° C was administered intravenously to minimize sympathectomy-induced vascular volume shifts.

The initial volume of 2-chloroprocaine was chosen based on each volunteer's height, and was 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. Chloroprocaine was chosen as the epidural anesthetic because it is rapidly metabolized in plasma. Systemic absorption of the anesthetic,[13] and subsequent recirculation to the brain, therefore was unlikely to influence centrally mediated thermoregulatory responses. Before induction of general anesthesia, the volunteers were observed for 30–60 min to assure hemodynamic stability.

The volunteers were anesthetized with isoflurane on each study day. Anesthesia was induced by inhalation of 3–4% isoflurane in 70% nitrous oxide and oxygen; thiopental and opioids were not administered. Vecuronium (10 mg) was administered intravenously to facilitate tracheal intubation; muscle relaxation was subsequently maintained by an infusion of vecuronium (Program 2 syringe pump; Becton Dickenson, Lincoln Park, NJ) adjusted to maintain zero to one twitch in response to supramaximal train-of-four electric stimulation of the ulnar nerve at the wrist. Nitrous oxide was discontinued after induction of anesthesia, and the trachea of each volunteer was intubated. Mechanical ventilation was adjusted to maintain an end-tidal P_{CO_2} near 35 mmHg. Anesthesia was maintained with isoflurane at an end-tidal concentration of 0.7% using a Modulus CD integrated anesthesia system (Ohmeda, Madison, WI). No airway heating or humidification was used.

Core hypothermia was induced *via* leg cooling by gradually reducing the temperature of the circulating-water mattress to 10° C. We continued cooling until fingertip thermoregulatory vasoconstriction was observed, and for one subsequent hour. The volunteers then were rewarmed by increasing the temperature of the circulating-water mattress to 42° C and adding a Bair Hugger forced-air warmer set on "high" (Model 420 lower body cover and Model 200 warmer; Augustine Medical, Eden Prairie, MN). During rewarming, the volunteers participated in a previously reported thermoregulatory protocol.[14] Isoflurane anesthesia then was discontinued, and each volunteer was allowed to recovery. After testing the sensory block level, the epidural infusion was stopped and the study ended.

Monitoring. Core temperature was measured in the distal one-fourth of the esophagus with a probe incorporated into an esophageal stethoscope (Mallinckrodt Anesthesia Products, St. Louis, MO). Area-weighted, upper body and lower body skin-surface temperatures were determined as previously described.[14] Core and skin-surface 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).

Heat flux from 15 skin-surface sites was determined as reported elsewhere.[4] We defined flux as positive when heat traversed skin to the environment. Thermal flux transducers measure heat lost *via* radiation, conduction, and convection. Transcutaneous and respiratory evaporative heat loss in nonsweating adults represents only a small fraction of basal metabolic heat production. Consequently, cutaneous thermal flux well represents total heat loss under the circumstances of this study. One W = 1 joule = 0.86 kcal/h; the specific heat of humans is ≈ 0.83 kcal $\cdot$ kg^{-1} $\cdot$ ° C^{-1}.[15]

Absolute right middle fingertip blood flow, resulting primarily from arteriovenous shunt flow,[16,17] was quantified using venous-occlusion volume plethysmography at 5-min intervals.[18] Volume plethysmography is considered the most reliable measure of extremity blood flow; we previously described our technique for determining finger blood flow in detail.[19] The vasoconstriction threshold was defined as the core temperature triggering a sudden decrease in finger blood flow. Toe blood flow was estimated using calf minus toe, skin-temperature gradients.[20] As in previous studies,[20] we considered a gradient of 4° C to indicate significant vasoconstriction.

Heart rate was monitored continuously using three-lead electrocardiography. Oxyhemoglobin saturation (S_pO_2) was measured continuously using pulse oximetry, and blood pressure was determined oscillometrically at 5-min intervals at the left upper arm using the Modulus CD Anesthesia System. Analog and serial thermoregulatory data were recorded at 5-min intervals, using a modification of a previously described data-acquisition system.[21] Anesthetic data were recorded using IdaCare, version 1.3 (Hermes System, P.I.R. Sart-Tilman, Belgium), which is Macintosh-based (Apple Computer, Cupertino, CA) patient information management software.

Data Analysis. The distal esophageal temperatures triggering vasoconstriction during isoflurane alone and combined epidural/isoflurane anesthesia were compared using two-tailed, paired *t* tests. The end-tidal isoflurane concentrations and upper- and lower-body skin

temperatures at the time of vasoconstriction also were compared using paired *t* tests. Finally, the decrease in cutaneous heat flux and the rates of core cooling after fingertip vasoconstriction were similarly compared. All values are expressed as mean ± SD; differences were considered significant when $P < 0.05$.

Patients

We studied 26 ASA Physical Status 1–3 patients aged 18–70 yr, undergoing colorectal surgery.

Protocol. The patients were premedicated with 0.25 mg atropine and 2.5 mg midazolam intramuscularly. After transfer to the operating room, they were randomly assigned to combined epidural/enflurane anesthesia or enflurane alone.

In patients receiving combined epidural/enflurane anesthesia, an epidural catheter was inserted *via* the T9–T10 or T10–T11 interspace. Four milliliters 1% lidocaine with 1/200,000 epinephrine was injected *via* the epidural catheter. A negative test dose was followed by epidural administration of 8 ml 0.5% bupivacaine. A continuous infusion of 0.25% bupivacaine at 8 ml/h was started 30 min later, and continued for the duration of surgery. Anesthetic was injected at ambient temperature, because we have previously demonstrated that injectate temperature does not alter thermoregulatory responses in nonpregnant subjects.[9,22]

General anesthesia was then induced in both groups by intravenous administration of 1 mg alfentanil and 5 mg/kg thiopental. Intubation of the trachea was facilitated by administration of 0.1 mg/kg vecuronium bromide. Mechanical ventilation was adjusted to keep end-tidal P_{CO_2} near 35 mmHg. Inspiratory gases were not warmed or humidified, and were administered *via* a nonrebreathing system. Anesthesia was subsequently maintained by administration of enflurane in 50% O_2/air. End-tidal enflurane concentration and fluid administration were adjusted to maintain a mean arterial pressure of 70–120 mmHg and a heart rate of 70–110 beats per min. Supplemental vecuronium was administered as needed to maintain one twitch in response to supramaximal train-of-four stimulation of the ulnar nerve at the wrist.

Patients wore antiembolism stockings, and were covered with a single cotton blanket during induction of anesthesia. At least 10 $ml \cdot kg^{-1} \cdot h^{-1}$ fluid was given intravenously, and all administered fluid was warmed to 37° C (Fenwal; Travenol Laboratories, Deerfield, IL). No patient was given blood products. Patients were not actively warmed during anesthesia, and passive insulation was restricted to a single layer of surgical drape.[23]

Monitoring. Ambient temperature was measured by a thermocouple positioned at the level of the patient, well away from any heat-producing equipment. Toe temperature was measured using a disposable thermocouple probe. Core temperature was measured at the tympanic membrane; tympanic membrane temperatures correlate well with distal esophageal temperatures during anesthesia.[20,24] The aural probe was inserted until patients felt the thermocouple touch the tympanic membrane; appropriate placement was confirmed when they easily detected a gentle rubbing of the attached wire. The probe was then securely taped in place and the aural canal occluded with cotton.

Fingertip blood flow was evaluated using forearm minus fingertip, skin-surface temperature gradients. There is an excellent correlation between skin-temperature gradients and volume plethysmography.[19] All temperatures were measured at 15-min intervals, using Mon-a-Therm thermometers and thermocouples.

Heart rate was monitored continuously using three-lead electrocardiography. Blood pressure was determined oscillometrically at 5-min intervals. Respiratory gas concentrations were quantified using a calibrated end-tidal gas analyzer (Capnomac; Datex Medical Instrumentation, Helsinki, Finland). The upper and lower levels of sensory blockade produced by epidural anesthesia was confirmed after emergence from general anesthesia by cold sensation.

The distal esophageal temperatures triggering vasoconstriction during enflurane alone and combined epidural/enflurane anesthesia were compared using two-tailed, paired *t* tests. The end-tidal enflurane concentrations and upper- and lower-body skin temperatures at the time of vasoconstriction were also compared using paired *t* tests. And, finally, the decrease in cutaneous heat flux and the rates of core cooling after fingertip vasoconstriction were similarly compared. All values are expressed as mean ± SD; differences were considered significant when $P < 0.01$.

Data Analysis. As in previous studies,[20,25,26] we considered a gradient of 4° C to indicate significant thermoregulatory vasoconstriction. The distal esophageal temperature triggering significant vasoconstriction was considered the vasoconstriction threshold.

Morphometric data, vasoconstriction thresholds, and the time of vasoconstriction were compared using two-tailed, unpaired *t* tests. As recommended by Matthews

et al.,[27] statistical analysis of the core temperature data was restricted to appropriate curve descriptors. Accordingly, we compared core temperatures in the two groups at 0, 1, 2, and 3 elapsed hours, using unpaired *t* tests. Additionally, the rates at which hypothermia developed during the first and last hour of anesthesia was calculated in each group using linear regression. All values are expressed as mean ± SD; differences were considered significant when $P < 0.05$.

Results

Volunteers

Induction of epidural anesthesia typically produced sensory blockade to the T8 dermatome (range T4–T11). During recovery from isoflurane anesthesia, the block level, typically, was T9 (range T5–L1).

Ambient, upper-body, and lower-body temperatures at the vasoconstriction threshold during isoflurane alone and combined epidural/isoflurane anesthesia are shown in table 1. End-tidal isoflurane concentrations at the thresholds are also shown in table 1. None of the parameters differed significantly during the two treatments.

The vasoconstriction threshold during isoflurane alone was 36.0 ± 0.2° C, but was significantly less during combined epidural/isoflurane anesthesia, 35.1 ± 0.7° C, a difference of 0.9 ± 0.6° C (fig. 1). After arm vasoconstriction, the calf minus toe, skin-temperature gradient increased to 3.2 ± 0.8° C within 30 min (indicating vasoconstriction). In contrast, the leg gradient remained −2.4 ± 0.7° C (indicating vasodilation) when the volunteers were given combined epidural/isoflurane anesthesia.

Table 1. Isoflurane Concentration and Temperatures

	Isoflurane Alone	Epidural–Isoflurane
Temperature		
Ambient (° C)	22.6 ± 0.6	23.2 ± 1.3
Lower body skin (° C)	28.7 ± 1.5	29.2 ± 0.6
Upper body skin (° C)	32.9 ± 0.9	31.7 ± 1.0
Isoflurane concentration (%)	0.69 ± 0.01	0.71 ± 0.02

Values are expressed as means ± standard deviations.

Data are ambient, upper body, and lower body temperatures at the vasoconstriction threshold during isoflurane alone and combined epidural–isoflurane anesthesia. End-tidal isoflurane concentration at the thresholds also are shown.

There were no statistically significant differences among the treatments.

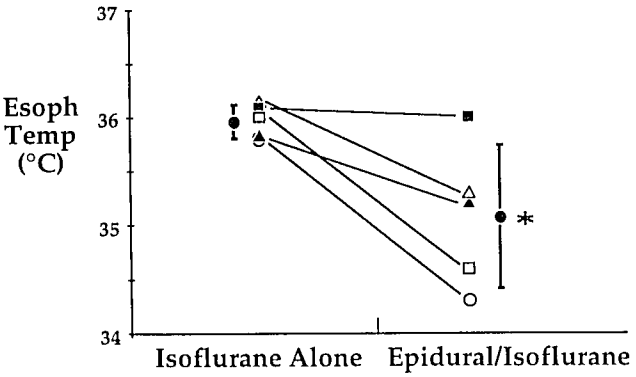

Fig. 1. The vasoconstriction threshold was 36.0 ± 0.2° C in the volunteers during isoflurane alone, and 35.1 ± 0.7° C during combined epidural/isoflurane anesthesia; a difference of 0.9 ± 0.6° C. *$P < 0.01$. Each symbol identifies a single volunteer.

Total cutaneous heat loss was similar 30 min before vasoconstriction with and without epidural anesthesia (121 ± 17 W and 117 ± 16 W, respectively). In the 30 min after vasoconstriction, heat loss decreased 33 ± 13 W when the volunteers were given isoflurane alone, but only 8 ± 16 W during combined epidural/isoflurane anesthesia ($P < 0.01$). Consequently, heat loss was greater during epidural/isoflurane anesthesia than during isoflurane alone. Not surprisingly, most of the difference was in the lower body, whereas changes in the upper body were comparable with and without epidural anesthesia (fig. 2).

The rates of core cooling were similar during the 30 min before vasoconstriction with and without epidural anesthesia (0.8 ± 0.3° C/h and 0.8 ± 0.2° C/h, respectively). However, the cooling rates in the subsequent 30 min were significantly greater during combined epidural/isoflurane anesthesia (0.8 ± 0.2° C/h) than during isoflurane alone (0.2 ± 0.1° C/h; fig. 3).

Patients

The gender, age, weight, and height of the patients in each group did not differ significantly. The ambient operating room temperature and fluid replacement volume also did not differ significantly in the two groups. The end-tidal enflurane concentration was significantly less in the patients given combined epidural/enflurane anesthesia than in those given only enflurane. Mean arterial blood pressures were similar in the two groups before surgery, but significantly greater during surgery in the patients given enflurane alone; however, the difference was not clinically important. Heart rates

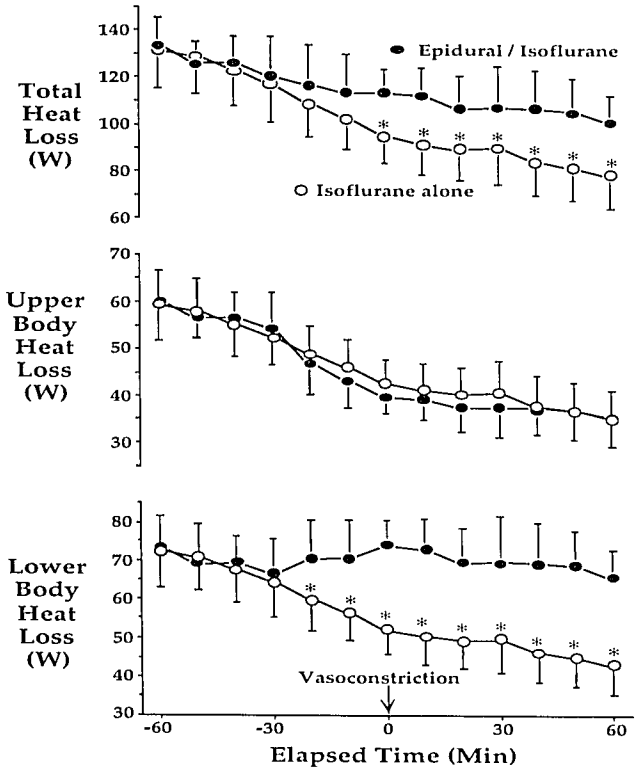

Fig. 2. Total cutaneous heat loss after vasoconstriction in the volunteers decreased significantly more when the volunteers were given isoflurane alone than when they were given combined epidural/isoflurane anesthesia. As might be expected, upper-body heat loss was similar during the two treatments, whereas differences were pronounced in the lower body. Elapsed time zero indicates the vasoconstriction threshold. *$P < 0.01$ between isoflurane alone and combined epidural/isoflurane anesthesia.

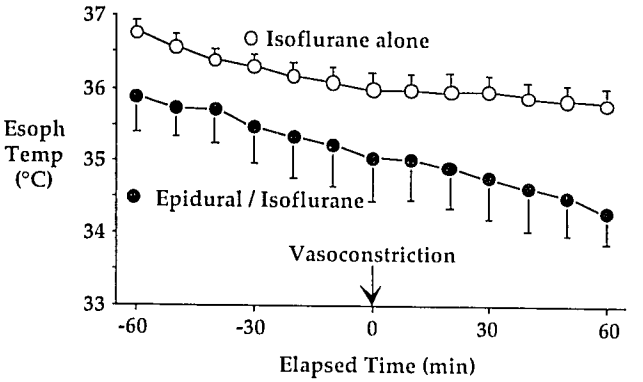

Fig. 3. Because the thresholds differed during isoflurane alone and combined epidural/isoflurane anesthesia, core temperatures in the volunteers at elapsed time zero (vasoconstriction) differed. The rates of core cooling were similar during the 30 min before vasoconstriction with and without epidural anesthesia (0.8 ± 0.3 and 0.8 ± 0.2° C/h, respectively). However, the cooling rates in the subsequent 30 min were greater during combined epidural/isoflurane anesthesia (0.8 ± 0.2° C/h) than during isoflurane alone (0.2 ± 0.1° C/h; $P < 0.01$).

were similar in the two groups (table 2). Surgery lasted at least 2.25 h in each patient, and 11 of 13 patients remained in each group after 3 elapsed hours. The epidural blocks extended cephalad to the 5th (±2) thoracic dermatome, and caudally to the 4th (±2) lumbar dermatome.

In nearly all of the patients, vasoconstriction (skin-temperature gradient > 4° C) was present at the time of anesthetic induction. In three patients in the epidural/enflurane group, vasoconstriction remained throughout surgery, and, in three, vasoconstriction never occurred during anesthesia. Similarly, in six patients given enflurane alone, vasoconstriction was present throughout surgery, while, in all the remaining patients, vasoconstriction occurred before the end of surgery. Among the patients in whom vasodilation was observed after induction of anesthesia, and in whom vasoconstriction subsequently occurred, the vasoconstriction threshold in the epidural/enflurane group (n = 7) was 34.5 ± 0.6° C, which was significantly less than that in the enflurane-only group (n = 7), 35.6 ± 0.8° C.

Toe temperature exceeded 30° C (an index of vasodilation) in 70% of the patients given combined epidural/general anesthesia. In contrast, toe temperature after vasoconstriction in the arms always was less than 30° C in the patients given enflurane alone.

Initial (preinduction) tympanic membrane temperatures were similar in the two groups. The initial rate

Table 2. Morphometric Data, Ambient Temperature, Enflurane Concentration, and Fluid Replacement

	Enflurane	Epidural–Enflurane
Age (yr)	54 ± 13	60 ± 13
Weight (kg)	69 ± 11	73 ± 11
Height (cm)	168 ± 8	173 ± 7
Gender (M/F)	7/6	6/7
Ambient temperature (° C)	20.7 ± 1.5	20.7 ± 1.5
End-tidal enflurane (%)	0.8 ± 0.2	0.6 ± 0.2*
Fluid replacement ($ml \cdot kg^{-1} \cdot h^{-1}$)	14 ± 4	16 ± 4
Mean arterial pressure (mmHg)	96 ± 11	82 ± 14*
Heart rate ($beats \cdot min^{-1}$)	77 ± 10	72 ± 11

Values are expressed as means ± standard deviations.

* $P < 0.05$ compared with the control group.

of core cooling was significantly greater in the epidural/enflurane group than in the patients given enflurane only. Distal esophageal temperatures were significantly less in the epidural/enflurane group than in the other patients, at 1, 2, and 3 elapsed hours. Despite their lower core temperatures, the rate of core cooling during the second to third elapsed hour was nearly four times greater in the epidural/enflurane group (fig. 4 and table 3).

Discussion

It is unlikely that regional anesthesia impairs centrally mediated thermoregulation either by direct transport of local anesthetics to the brain in cerebrospinal fluid or *via* recirculation of epidurally administered drug in blood. Inhibition was observed in the patients given epidural anesthesia, just as it has been during spinal anesthesia,[10,11] although the amount and location of administered local anesthetic differed markedly. Similar inhibition is also reported in patients with spinal cord transections.[28] Furthermore, intravenous administration of lidocaine in doses sufficient to produce plasma concentrations typically occurring during epidural anesthesia does not alter thermoregulation.[13] And, finally, the vasoconstriction threshold in the volunteers was also reduced $\approx 1°$ C, despite our use of 2-chloroprocaine, a drug that is rapidly metabolized in plasma.

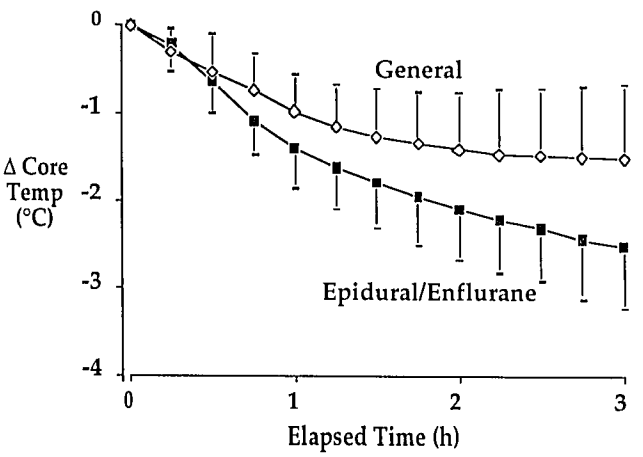

Fig. 4. Intraoperative core temperature in patients given enflurane anesthesia alone decreased rapidly for 75 min, and then remained relatively constant for the duration of surgery. In contrast, core temperature in patients given combined epidural/enflurane anesthesia continued to decrease throughout the study. Consequently, core temperatures differed by 1.2° C after 3 h of anesthesia and surgery ($P < 0.05$). Data are presented as mean ± SD.

Table 3. Initial and Intraoperative Temperatures and Rates of Core Cooling

	Enflurane	Epidural–Enflurane
Core temperature (° C)		
Initial	36.6 ± 0.4	36.5 ± 0.3
1 h	35.6 ± 0.4	35.1 ± 0.5*
2 h	35.2 ± 0.7	34.4 ± 0.6*
3 h	35.1 ± 0.8	33.9 ± 0.7*
Cooling rate (° C/h)		
0–1 h	1.0 ± 0.3	1.4 ± 0.4*
2–3 h	0.1 ± 0.3	0.4 ± 0.2*
Constriction threshold (° C)	35.6 ± 0.8	34.5 ± 0.6*
Time of constriction (h)	1.2 ± 0.8	2.0 ± 0.4*

Values are expressed as means ± standard deviations.

* $P < 0.05$ compared with the control group.

The significant reduction in the vasoconstriction threshold we now report during combined epidural/general anesthesia contrasts to our previous report that caudal anesthesia had little influence on vasoconstriction during general anesthesia.[29] In our study of the thermoregulatory effects of caudal anesthesia, we evaluated infants and children, rather than adults, and gave halothane instead of isoflurane. However, neither of these factors seems to be a sufficient explanation for the divergent results. Most likely, the effects of caudal anesthesia were insignificant because the very low, and, presumably, segmental, block minimally altered peripheral thermal input to the regulatory system.

A potential explanation for the reduced vasoconstriction threshold in patients given combined epidural/enflurane anesthesia is that the nerve block prevented transmission of surgical pain. Painful electric stimulation during enflurane anesthesia, 1.3% end-tidal concentration, increases the vasoconstriction $\approx 0.4°$ C.[30] Although 0.4° C is considerably less than the observed difference in the thresholds, surgical pain is certainly more intense than intermittent electric stimulation. Furthermore, painful stimulation—of any magnitude—may have greater thermoregulatory consequences at the relatively low anesthetic concentrations that we used in this study. Nonetheless, the threshold was comparably reduced by epidural anesthesia in the nonsurgical volunteers. These data indicate that differences in stimulation are not a sufficient explanation for the observed thermoregulatory effects of regional anesthesia.

It proved impossible to achieve our blood pressure targets and administer the same enflurane concentration

to each group. Consequently, the patients given enflurane alone received 0.8 ± 0.2% enflurane, whereas those given combined epidural/general anesthesia received only 0.6 ± 0.2%. The dose-response relationship for thermoregulatory impairment during enflurane anesthesia remains unknown, but is roughly linear during isoflurane.[20,31] To the extent that a linear extrapolation is reasonable during enflurane anesthesia, one would expect the epidural group to vasoconstrict at a core temperature ≈0.5° C greater than in patients given enflurane only. Nonetheless, when epidural and enflurane anesthesia were combined, vasoconstriction occurred at core temperatures ≈ 1° C *less* than during enflurane anesthesia alone. The reduced vasoconstriction threshold during combined epidural/enflurane anesthesia is unlikely to result from direct inhibition of sympathetic nerves supplying the arm, because most patients eventually did constrict.

We previously demonstrated that the vasoconstriction threshold in surgical patients was inversely proportional to the end-tidal isoflurane concentration, and was related by the regression equation: Threshold (° C) = 37.1 − 3.1 × (isoflurane); r = −0.97.[20] Thresholds reported in several other studies are generally consistent with this equation.[4,32] From this equation, vasoconstriction without epidural anesthesia may be expected at ≈35° C, whereas the observed threshold was ≈36° C. One difference between the studies is that we previously studied surgical patients, rather than volunteers. However, painful stimulation slightly *increases* vasoconstriction thresholds,[30] and, thus, fails to explain the differing results.

Both skin and core temperatures contribute to thermoregulatory responses.[33,34] (It is this cutaneous thermoregulatory input that stops shivering when the skin is warmed in hypothermic postoperative patients.[35,36]) Because active cutaneous cooling in the current study reduced skin temperature, we would expect the regulatory system to tolerate somewhat less core hypothermia before initiating protective thermoregulatory vasoconstriction (*i.e.,* the vasoconstriction threshold would be higher). In contrast, we cooled our surgical patients by infusion of cold saline,[20] a process producing core hypothermia while leaving skin temperature relatively high. Additionally, thresholds are slightly higher when defined by initiation of vasoconstriction (as they were in the volunteers) than by completion of the response. In any case, the same methods and definitions were used on each day of this study; the observed differences induced by epidural anesthesia thus remain valid, irrespective of comparisons with previous work.

As expected in a cool operating room environment, vasoconstriction was observed in nearly all patients before induction of anesthesia. Induction of anesthesia activates the sympathetic nervous system, which apparently was sufficient to maintain vasoconstriction for about 30 min in most patients. Induction of anesthesia also rapidly reduced core temperature. Consequently, it is not surprising that about one-half of the patients given 0.8% end-tidal enflurane as the sole anesthetic reached their vasoconstriction thresholds within this period, and, thus, never demonstrated vasodilation during surgery. In the others, vasodilation occurred briefly before they reached their thresholds and vasoconstriction was then observed for the remainder of surgery. In contrast, all but three patients having combined epidural/enflurane anesthesia demonstrated vasodilation after induction of anesthesia.

Cutaneous heat loss in the volunteers given isoflurane anesthesia alone decreased ≈40% in the period from 1 h before vasoconstriction to 1 h after constriction. This value is nearly twice that reported previously by us,[4] a difference presumably resulting because, in this study, we actively cooled the legs, thereby increasing the efficacy of peripheral vasoconstriction. In contrast to isoflurane alone, heat loss remained high during combined epidural/isoflurane anesthesia, and actually increased slightly in the legs. Heat flux differences (in the lower body) became apparent ≈30 min before arm vasoconstriction was detected, which is consistent with the observation that leg vasoconstriction precedes constriction in the arms (*i.e.,* has a slightly higher threshold).[20]

The initial rate of core cooling was slightly, but statistically significantly, greater in the patients given combined epidural/enflurane anesthesia than in those given enflurane alone (1.0 *vs.* 1.4° C/h). Although the major cause of core hypothermia during the first hour of anesthesia is usually internal redistribution of body heat,[1] cutaneous heat loss certainly contributes. Increased cooling may have resulted from facilitated redistribution, augmented cutaneous heat loss, or a combination of the two. We did not evaluate the relative contribution of each mechanism in these patients.

Because leg vasoconstriction was both centrally impaired and prevented peripherally, neither the volunteers nor the patients developed a normal core-temperature plateau during combined epidural/general anesthesia; the rate of core cooling after peripheral va-

soconstriction without epidural blockade was one-third to one-quarter of that during combined epidural/general anesthesia. These data reinforce the importance of vasoconstriction in maintaining core temperature. Temperature monitoring and thermal management[2,37] may be particularly important in patients whose ability to vasoconstrict is impaired by regional anesthesia or neurologic disease.

In summary, it already is established that regional anesthesia decreases the core temperature, triggering thermoregulatory vasoconstriction and shivering (above the level of the block). Our data indicate that the threshold for thermoregulatory vasoconstriction is also reduced during combined epidural/general anesthesia, compared with that during general anesthesia alone. Furthermore, epidural anesthesia directly inhibits its vasoconstriction in the legs, preventing the normal process by which thermoregulation usually minimizes intraoperative core hypothermia. The combination of directly and centrally mediated thermoregulatory impairment during combined regional/general anesthesia thus significantly aggravates hypothermia compared with general anesthesia alone. Temperature monitoring and thermal management may be particularly important in patients in whom regional and general anesthesia is combined.

The authors wish to thank Ohmeda for the loan of a Modulus CD integrated anesthesia machine; Mallinckrodt Anesthesia Products, for donation of the thermocouples used in this study; Datex Medical Instrumentation, for the loan of a Capnomac anesthetic gas monitor; Becton Dickenson, for the loan of a Program 2 syringe pump; Hermes Systems for the loan of a IdaCare automatic record-keeping system; Cincinnati Sub-Zero, for the loan of a Blanketrol II circulating-water warmer; and Anaquest, for the generous donation of the isoflurane used in this study.

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