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## Metabolic Changes during Recovery in Normothermic versus Hypothermic Patients Undergoing Surgery and Receiving General Anesthesia and Epidural Local Anesthetic Agents

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**Background:** Mild hypothermia is accompanied by metabolic changes. Epidural local anesthetic agents attenuate the surgical stress response, but it is not known whether they modulate thermal stress.

**Methods:** Thirty patients undergoing colorectal surgery, performed by one surgical team, received epidural 0.5% bupivacaine to achieve T3-S5 sensory block. They were then assigned randomly to two groups of 15 patients each. The control or unwarmed group was left to cool during surgery, whereas active warming was used in the warmed group. General anesthesia was induced by thiopentone, vecuronium, fentanyl, nitrous oxide in oxygen, and enflurane. At the end of surgery, both groups received epidural 0.25% bupivacaine to maintain a T5-L3 sensory block. Aural canal (core) and skin surface (15 sites) temperatures; oxygen consumption; pain visual analogue score; and concentrations of epinephrine, norepinephrine, glucose, cortisol, lactate, and free fatty acids in plasma were measured before epidural blockade, 30 min after epidural blockade, at the end of surgery, and for 4 h after surgery. Patients and those measuring the outcomes were unaware of group allocation.

**Results:** Core and mean skin temperatures decreased significantly in the control group ( $P < 0.001$ ) but not in the

warmed group. Catecholamine concentrations in plasma decreased significantly after epidural block, and although concentration of epinephrine in plasma increased from baseline sharply in the control group at the end of surgery ( $P = 0.004$ ), it decreased in the warmed group ( $P = 0.007$ ). During recovery, there was no difference between the two groups for norepinephrine concentrations in plasma, body weight-adjusted oxygen consumption, pain visual analogue score, and metabolites.

**Conclusions:** The postoperative metabolic changes obtained with epidural block were similar except for an attenuated concentration of epinephrine in normothermic patients compared with those who were mildly hypothermic. (Key words: Catecholamines; core temperature; skin temperature; sympathetic nervous system.)

A PERIOPERATIVE, nonintentional, decrease in body temperature by  $\approx 2^\circ\text{C}$  is commonly observed during major abdominal surgery. This mild hypothermia has been associated with several immediate postoperative metabolic consequences, such as shivering. This is responsible for elevated sympathoadrenal discharge and increased oxygen demand.<sup>1,2</sup> This cascade of events can contribute to a greater incidence of myocardial ischemia reported during the postoperative period.<sup>3</sup> The side effects of perioperative hypothermia seem to extend beyond the immediate postoperative period with impairment of immune function,<sup>4</sup> increased susceptibility to wound infection,<sup>5</sup> and enhanced muscle protein breakdown.<sup>6</sup>

Perioperative nociceptive deafferentation with local anesthetic agents attenuates the exaggerated endocrine and metabolic response associated with surgery<sup>7</sup> and induces peripheral vasodilation.<sup>8</sup> Epidural blockade is responsible for a decrease in core temperature and a redistribution from the core to the periphery. It interferes also with afferent thermosensory input from the muscle and skin.<sup>9</sup>

Epidural blockade with local anesthetic agents insti-

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tuted before or at the end of major abdominal surgery and aimed to attenuate the metabolic response to moderate hypothermia showed a significant suppression of concentration of catecholamines in plasma and minimal changes in oxygen consumption.<sup>1,10</sup> These investigations included only patients undergoing surgery, and the thermal stress response measured was over and above the surgical stress response. The current study was designed to verify whether mild hypothermia would trigger a metabolic stress response during the immediate postoperative period in the presence of epidural blockade with local anesthetic agents.

## Methods and Materials

### *Patients*

The study was approved by the institutional ethics committee of the Royal Victoria Hospital, and written informed consent was obtained from all patients. Thirty patients diagnosed with benign or malignant tumor of the colon and scheduled for elective colonic resection were studied. None suffered from inflammatory bowel disease, malnutrition, recent significant weight loss, anemia, morbid obesity, or endocrine disorders, and none had a pyrexia. The study was double-blinded: Patients and those assigned to measure outcome were not aware of group allocation.

### *Anesthesia and Surgical Care*

No premedication was administered. At arrival in the operating room, the patient was placed in a sitting position, and an epidural catheter was inserted in the T9 interlumbal space during aseptic conditions. After a test dose of 3 ml of 2% lidocaine, 10–15 ml of 0.5% bupivacaine was injected to produce a bilateral segmental sensory block to ice cold and pin prick from T3–S5. Once the block was established, they were randomly allocated to two groups of 15 patients each. In the control or unwarmed group, body temperature was allowed to decrease during surgery and recovery, and no measures were taken to maintain normothermia unless core temperature was  $<33.5^{\circ}\text{C}$ , in which case patients were to be excluded from the study, but it did not happen. In contrast, patients in the treatment group (warmed) had their core and skin temperatures maintained at preoperative levels throughout the perioperative period. This was achieved by active warming of the intravenous fluids at  $37^{\circ}\text{C}$  with a blood warmer and application of a convective warm air blanket (Mallinckrodt Medical Inc.,

St. Louis, MO) set at  $42^{\circ}\text{C}$  over the exposed skin surface of the trunk, limbs, and head once the epidural block was achieved and during and after surgery.

General anesthesia was then induced in both groups with thiopentone and maintained with 100  $\mu\text{g}$  fentanyl and 0.4% end-tidal isoflurane. Muscle relaxation was achieved with vecuronium. The lungs were ventilated at normocapnia with a mixture of 66% nitrous oxide in oxygen. Further bolus doses of 5 ml of 0.5% bupivacaine were injected every 60 min throughout surgery. Preservative-free morphine (2–3 mg) was injected in the epidural space in all patients. At the end of surgery, the trachea was extubated and the patients transferred to the recovery room, where the segmental sensory block was assessed at arrival and every 30 min. If it was below T7 or above L3 dermatomes, bolus doses of 5 ml of 0.25% bupivacaine were administered. At the end of the 4 h study, they were sent to the surgical wards, and analgesia was provided by intermittent epidural injection of preservative-free morphine (range, 3–5 mg; 6–8 hourly) as used in this institution. This regimen was continued for 3 days, after which pain relief was provided with orally administered codeine and acetaminophen.

All patients in the two groups received an infusion of 0.9% NaCl throughout the study period set at a rate of  $6\text{--}8\text{ ml}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ . Hypotension (arterial systolic blood pressure  $<80\text{ mmHg}$ ) was treated with incremental doses of 0.1 mg phenylephrine. Antibiotic prophylaxis consisted of 1 g cefoxitin and 500 mg metronidazole administered intravenously before surgical incision. All operations were performed by one surgical team in the early afternoon. The incidence of shivering was assessed in the recovery room by a nurse unaware of the study and recorded on a 3-point scale (0 = none, 1 = mild, 2 = severe).

### *Temperature Measurements*

On arrival in the operating room and before the insertion of an epidural catheter, a thermocouple probe (Mono-a-therm; Mallinckrodt Medical) was inserted in the aural canal, positioned adjacent to the tympanic membrane, and secured with cotton-wool to avoid drafts, thus measuring core temperature. Skin temperature was recorded at 15 sites located in the forehead, cheek, neck, nipple, midarm, midforearm, dorsum of the hand, umbilicus, iliac crest, medial thigh, lateral thigh, knee, medial calf, lateral calf, and dorsum of the foot with an infrared thermometer previously described.<sup>11</sup> The mean unweighted skin temperature was



calculated from the 15 sites.<sup>12</sup> All probes and thermometers were accurate to 0.1°C. Tympanic (core) and skin temperatures were measured before epidural block (baseline), 30 min after the bilateral segmental neural blockade was achieved, before general anesthesia (post-epidural), at the end of surgery, before transfer to the recovery room (end surgery), and subsequently every hour for 4 h, for a total of seven points in time. Ambient temperature also was measured in the operating room and the recovery room at those time intervals using a mercury-in-glass thermometer. Relative humidity was between 35% and 42%.

#### *Gaseous Exchange*

Measurements of oxygen consumption ( $\text{VO}_2$ ) and carbon dioxide production ( $\text{VCO}_2$ ) were performed by the open-circuit method of indirect calorimetry (Deltatrac; Datex, Helsinki, Finland), regularly calibrated. The measurements were undertaken with patients lying in a semirecumbent position (20°), breathing room air in the ventilated hood, for 20 min on each occasion. An average value was taken, with a coefficient of variation <10%. The measurements were taken at the same time intervals as the body temperature omitting the measurement at the end of surgery. This time point was considered inappropriate because of the unstable cardiorespiratory conditions and the residual effect of anesthetic gases.

#### *Visual Analogue Score and Motor Block*

Pain at rest and on coughing was assessed during recovery on an hourly basis using a 1- to 100-mm scale. Motor block was also assessed using a modified Bromage score.

#### *Blood Sampling*

Blood samples were collected from an indwelling radial artery cannula, placed in an aseptic condition before the commencement of the study. Patients were then allowed to rest for a minimum of 30 min, after which blood was withdrawn at the following times: baseline, postepidural block, end of surgery, before the extubation of the trachea, and subsequently every hour for 4 h. The blood was immediately centrifuged at 4°C and the supernatant stored at -30°C for the period of the study. At the end of the day, the samples were transferred to a -70°C freezer to wait for analysis of concentrations of epinephrine, norepinephrine, cortisol, glucose, lactate, and free fatty acids in plasma.

An aliquot of the blood withdrawn was analyzed for

acid-base balance (arterial oxygen tension, arterial carbon dioxide tension, and arterial oxygen saturation [ $\text{SaO}_2$ ]) before surgery and 1 h after the end of surgery.

#### *Biochemical Assays*

Concentrations of epinephrine and norepinephrine in plasma were determined using high-performance liquid chromatography. Alumina extraction was achieved using the Bio-Rad HPLC kit (Bio-Rad Laboratories Ltd, Mississauga, Ontario, Canada). The mean intraassay coefficients of variance for epinephrine and norepinephrine were 5.25% and 3.35%, respectively. The mean interassay coefficients of variance for epinephrine and norepinephrine were 4.65% and 2.8%, respectively.

Concentrations of cortisol in plasma were measured using the Ciba Corning ACS 180 automated immunoassay (Ciba Corning Diagnostic Corp, East Walpole, MA). The mean intraassay and interassay coefficients of variance were 3.0% and 7.7%, respectively.

Concentrations of glucose in plasma was measured by a glucose-oxidase method using a glucose analyzer 2 (Beckman Instruments, Fullerton, CA). Plasma lactate assay was based on lactate oxidase and was performed using the Synchron CX 7 system (Beckman Instruments). The mean intraassay and interassay coefficients of variance were 3.0% and 4.5%, respectively.

Free fatty acids in plasma were measured using the Boehringer Mannheim colorimetric enzymatic kit (Boehringer Mannheim, Laval, Quebec, Canada). The mean intraassay and interassay coefficients of variance were 2.3% and 4.1%, respectively.

#### *Statistical Analysis*

The number of patients required was based on very similar previous studies<sup>1,10</sup> that had enough power to detect statistically significant differences between control and warmed groups using essentially the same statistical methods. The current study differs from those studies in that epidural blockade was administered to both groups before surgery.

Paired *t* tests, when appropriate, were used to compare baseline measurements with those at the end of surgery. Comparisons between the demographic and clinical characteristics and clinical outcomes of the two groups were analyzed using a *t* test, Wilcoxon's rank sum test, or chi-square analysis as appropriate.

For comparison of treatments from the end of surgery onward, a repeated-measures analysis of variance was applied to temperature measurements, metabolic measurements, and the pain visual analogue scale.<sup>13</sup> Treatment com-



**Table 1. Demographic Characteristics and Clinical Data of Patients Studied**

	Control (n = 15)	Warmed (n = 15)	P Value (2-sided)
Age (yr)	60 ± 3.4	64 ± 5.6	0.17
Sex (F:M)	6:9	9:6	0.27
Weight (kg)	78 ± 6.6	61 ± 5.4	0.001
Height (cm)	171 ± 3.7	166 ± 4.3	0.11
ASA (1:2)	11:4	6:9	0.07
Duration of surgery (min)	173 ± 23	172 ± 22	0.94
Shivering (0:1:2)	9:5:1	11:4:0	0.3 (Wilcoxon)
Blood loss (ml)	317 ± 130	270 ± 59	0.52
Crystalloids (ml) during surgery and recovery	5,200 ± 668	4,433 ± 457	0.08
0.5% bupivacaine (ml) intraoperatively	22.5 ± 2.9	22.3 ± 2.9	0.92
0.25% bupivacaine (ml) postoperatively (0–4 h)	11.5 ± 1.6	7.9 ± 1.8	0.006

Values are either the observed mean ± SEM or frequencies for a chi-square test. The *P* values are from a *t* test or an "uncorrected" chi-square test, respectively.

parisons were made among patients, whereas time comparisons were made within patients. Time-effect trends were subdivided into orthogonal polynomial contrasts (linear, quadratic, and cubic). Covariates, such as dose of bupivacaine, sex, and body weight, were included if they had a significant modifying effect on treatment difference. The computer program BMDP5V (BMDP Statistical Software, Los Angeles, CA) was used to perform the analysis of variance, using maximum likelihood estimation.<sup>14</sup> Unlike similar procedures, BMDP5V does not impose covariance restrictions. The best fitting models were determined through Akaike's information criterion, after deleting polynomial factors, covariates, and interactions for which the likelihood ratio test yielded probability values >0.10. Tests of the assumption of normality<sup>15</sup> were applied to standardized residuals of analysis of variance models. No models violated the assumption.

## Results

The characteristics of the patients studied, together with the clinical data, are presented in table 1. Types of colonic surgery included left hemicolectomy, sigmoid resection, anterior resection, and colectomy, which were equally distributed between the two groups. Body weight was significantly greater in the control group.

The requirement of epidural bupivacaine to maintain adequate segmental sensory blockade after surgery was marginally greater in the control group than in the warmed group (*P* = 0.006). Both groups received a similar amount of morphine, corrected by body weight at the end of surgery (*P* = 0.94).

An average of 4 (range, 0–11) bolus doses of 0.1 mg phenylephrine were required during the initial intraoperative period of the study to maintain arterial systolic blood pressure >80 mmHg. There was no need for vasopressor during the postoperative period.

### Body Temperature

Baseline core and mean skin temperatures (table 2) were similar in both groups. Thirty minutes after the epidural block was established, core temperature remained unchanged, whereas mean skin increased significantly in the warmed group. These temperatures decreased significantly with surgery in the control group (*P* < 0.001), whereas they either remained unchanged or increased in the warmed group for core (*P* < 0.05) and for skin (*P* < 0.001) temperatures. The results of analysis of variance showed treatment differences for core and mean skin temperatures from the end of surgery onward. There were significant trends over time in postoperative core and mean skin temperatures with differences between the groups (core, *P* < 0.001; mean skin, *P* < 0.001). Baseline dorsum hand and foot temperatures were similar in both groups. Dorsum hand temperature decreased after epidural block in the control group and remained unchanged with surgery and recovery. In contrast, it increased in the warmed group (*P* < 0.01). There was a significant difference between the two groups throughout the study period. Dorsum foot temperature increased in both groups after epidural block because of vasodilation; however, this was greater in the warmed group (*P* < 0.001). Operating room and recovery room temperatures were similar in both groups.

### Visual Analogue Scale

There was no significant difference in pain visual analogue scale at rest and on coughing between the two groups during the recovery period (table 2). Motor block during the first 4 h after surgery ranged between 1 and 3 in both groups, confirming the similar extent of neural blockade.

### Spread of Sensory Block

Spread of sensory blockade from T3 to S5 dermatomes was achieved in all patients before surgery and maintained throughout. A less extensive block (median up-



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**Table 2. Clinical Data on Mean Core, Skin and Room Temperature, Gaseous Exchange, and VAS in the Two Groups Studied (Group C = 15, Group W = 15) (Polynomial Repeated Measures ANOVA)**

	Baseline	Postepidural	End of Surgery	R1	R2	R3	R4	Est SE	P Values	
									Group	Group × Time
Core temp (°C)										
C	36.8	36.4	35.2	34.9	36.0	36.4	36.7	0.194	<0.001	>0.2
W	36.9	36.6	36.6	36.7	36.9	37.2	37.0			
Mean skin temp (°C)										
C	33.1	33.2	31.6	32.4	32.8	32.9	33.1	0.246	<0.001	>0.2
W	33.4	35.1	34.6	35.3	35.2	35.6	35.6			
Dorsum hand temp (°C)										
C	30.7	29.9	29.0	28.2	28.1	29.0	28.5	0.429	<0.001	>0.2
W	30.6	32.8	34.8	33.8	33.0	33.2	33.7			
Dorsum foot temp (°C)										
C	30.3	32.2	32.6	32.3	32.0	31.8	32.0	0.370	<0.001	<0.002
W	31.4	35.4	34.9	35.4	36.3	36.3	36.0			
Room temp (°C)										
C	23.0	22.3	22.4	23.1	23.2	23.5	23.4	0.156	>0.2	>0.2
W	22.3	22.5	22.9	23.3	23.5	23.5	24.2			
VAS (at rest) (mm)										
C				8	7	10	6	2.23	>0.2	>0.2
W				10	9	12	6			
VAS (on coughing) (mm)										
C				16	18	23	17	2.85	>0.2	>0.2
W				23	21	23	19			

Est SE = average of estimate of standard error for the best fitting model, so a 95% confidence interval is roughly a mean estimate  $\pm 1.96 \times$  Est SE; C = control group; W = warmed group; VAS = visual analogue scale; R1–R4 = hours after end of surgery; temp = temperature.

per and lower sensory levels, T5–L3; upper level range, T4–T7; lower level range, L2–S1) continued during the 4 postoperative hours. There was no difference between the two groups.

#### Gaseous Exchange

The values for oxygen consumption ( $\text{VO}_2$ ) and carbon dioxide production ( $\text{VCO}_2$ ) have been corrected by dividing by body weight, as this was the only statistically significant covariate (table 3). There were no significant differences between the two groups in the corrected oxygen consumption, carbon dioxide production, and RQ throughout the study period. In addition, no significant time interaction was observed. Corrected oxygen consumption decreased in the warmed group after the epidural blockade ( $P = 0.006$ ), however. No difference in gas exchange was

observed between the patients in the control group who shivered and those who did not.

#### Concentrations of Catecholamines in Plasma

Baseline circulating concentrations of epinephrine and norepinephrine in plasma were similar in both groups (table 3). This was followed by a significant decrease in plasma concentrations 30 min after the epidural block ( $P < 0.005$ ). Concentration of epinephrine in plasma increased significantly at the end of surgery in the control group ( $P = 0.004$ ), whereas it decreased in the warmed group ( $P = 0.007$ ). In particular, the concentration increases sharply after surgery in the control group and remained elevated for the next 4 h, whereas the concentration in plasma in the warmed group did not change immediately after surgery but increased hour by hour in a linear



**Table 3. Mean Plasma Concentrations of Hormones and Metabolites of the Two Groups Studied (Group C = 15, Group W = 15) (Polynomial Repeated Measures ANOVA)**

	Baseline	Postepidural	End of Surgery	R1	R2	R3	R4	Est SE	P Values	
									Group	Group × Time
VO <sub>2</sub> (ml · min <sup>-1</sup> · kg <sup>-1</sup> )										
C	3.0	3.1		3.3	3.1	3.2	3.3	0.086	>0.2	>0.05
W	3.3	3.1		3.4	3.3	3.3	3.3			
VCO <sub>2</sub> (ml · min <sup>-1</sup> · kg <sup>-1</sup> )										
C	2.3	2.3		2.4	2.3	2.5	2.5	0.088	>0.09	>0.2
W	2.4	2.3		2.2	2.4	2.4	2.6			
R/Q										
C	0.74	0.74		0.71	0.75	0.75	0.77	1.08	>0.2	>0.1
W	0.72	0.74		0.67	0.74	0.73	0.75			
Epinephrine (pM)										
C	340	253	545	450	417	462	579	38	<0.001	<0.001
W	350	234	211	340	389	533	612			
Norepinephrine (pM)										
C	1,648	1,355	1,409	1,719	1,580	2,076	2,367	131.2	>0.2	>0.2
W	1,728	1,350	1,696	1,622	1,698	1,686	1,859			
Cortisol (nM)										
C	403	430	682	834	800	849	688	58.3	>0.2	>0.2
W	350	331	693	764	769	767	742			
Glucose (mM)										
C	5.6	5.7	6.9	7.6	7.3	7.2	7.1	0.339	>0.2	>0.2
W	5.4	5.2	6.4	6.7	6.7	7.0	6.9			
Lactate (mM)										
C	0.7	0.7	0.9	1.1	1.1	1.2	1.1	0.097	>0.05	>0.2
W	0.7	0.6	0.7	0.6	0.7	0.6	0.6			
FFA (mM)										
C	0.82	0.83	0.66	0.69	0.64	0.64	0.69	0.023	>0.2	>0.1
W	0.82	0.72	0.63	0.63	0.68	0.73	0.69			

Est SE = average of estimate of standard error for the best fitting model, so a 95% confidence interval is roughly a mean estimate  $\pm 1.96 \times$  Est SE; C = control group; W = warmed group; FFA = free fatty acids; R1–R4 = hours after end of surgery; VO<sub>2</sub> = oxygen consumption; VCO<sub>2</sub> = carbon dioxide production.

fashion toward the level of the control group. There was a significant time and treatment interaction ( $P < 0.001$ ), characterized by the nonoverlap at the end of surgery of the 95% confidence intervals. Concentrations of norepinephrine in plasma remained unchanged with surgery, and there was no significant time effect or difference between the two groups ( $P > 0.20$ ).

#### *Concentrations of Cortisol, Glucose, Lactate, and Free Fatty Acids in Plasma*

The concentration of cortisol in plasma at baseline and after epidural block was similar in both groups

(table 3). There was a significant increase in the concentration with surgery in both groups ( $P < 0.0001$ ), and this remained elevated in the postoperative period, with no difference between the two groups.

The concentration of glucose in plasma increased significantly with surgery in both groups ( $P < 0.0001$ ) and remained elevated, with no significant difference between the two groups. Circulating concentrations of lactate did not change significantly during and after surgery in either group ( $P = 0.29$ ). The concentration of free fatty acids in plasma decreased significantly in both groups ( $P < 0.006$ ) and remained unchanged thereafter.



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*Arterial Oxygen Tension, Arterial Carbon Dioxide Tension, and SaO<sub>2</sub>*

No significant differences were observed in acid-base status between the two groups throughout the study period.

## Discussion

Colonic surgery during epidural blockade with additional general anesthesia is responsible for a significant decrease in body temperature. Despite a significant decrease in body temperature, no metabolic disturbances were found, except for concentration of epinephrine in plasma, which was elevated at the end of surgery. The adrenergic response was mild, however, and was not accompanied by significant changes in concentrations of norepinephrine in plasma, gas exchange, and gluconeogenic metabolites.

The decrease in body temperature observed in the control group was of a similar magnitude as previously reported when either epidural blockade with local anesthetic agents was used in conjunction with general anesthesia<sup>1</sup> or when general anesthesia was used alone.<sup>1</sup> Regional anesthesia obviously blocks all thermoregulatory response in the blocked area.<sup>16,17</sup> Epidural anesthesia, however,<sup>18,19</sup> also decreases the thresholds of vasoconstriction and shivering. This decrease seems related to an apparent increase in leg skin temperature<sup>20</sup> and depends on block height.<sup>21</sup> Similarly, epidural anesthesia decreases the perception of cold,<sup>22</sup> with the result that hypothermic patients undergoing surgery often fail to recognize that they are cold.<sup>23</sup> Recent studies in volunteers,<sup>24</sup> confirmed by the current findings, have demonstrated that the sympathetic block achieved with epidural local anesthetic agents is confined to the lower limbs, leaving the upper limbs vasoconstricted. The small decrease in core temperature results from redistribution of body heat from the core to the periphery. General anesthesia, in contrast, is associated with uniform redistribution of body heat and a greater decrease in core temperature, which is dependent on the minimum alveolar concentration of the inhalational agent used.<sup>25,26</sup> As our patients received both epidural and general anesthesia, it is not surprising that the decrease in core temperature was of the same magnitude reported with general anesthesia.

The baseline circulating concentrations of catecholamines in both groups were greater than those reported in previous studies<sup>1,2</sup> in which premedication was used.

The establishment, in the current study, of an extended epidural blockade for an average of 30 min before surgery was associated with a decrease in concentrations of epinephrine and norepinephrine in plasma, confirming the effectiveness of the sympathetic block, and this was not dependent on whether the patients were receiving active warming.

Great attention was paid during the intraoperative period to maintain an adequate neural afferent blockade extending from upper thoracic to lower sacral dermatome by administering regular doses of bupivacaine in both groups. Nevertheless, the circulating concentrations of epinephrine at the end of surgery in the control group were significantly elevated. The difference in concentrations of epinephrine in plasma between the warmed and the control group was remarkably smaller than the difference found in the previous study. This is in contrast to the much greater magnitude of change in values for concentrations of catecholamines in plasma observed in patients receiving general anesthesia without epidural blockade, in which epinephrine increased twofold and norepinephrine threefold.<sup>1,2</sup>

An unexpected noteworthy finding was the significantly greater amount of local anesthetic agent needed after surgery in the control or unwarmed group to provide adequate sensory level around the surgical area (T5-L3). A closer analysis reveals that these patients received most of the 0.25% bupivacaine during the first 2 h. As shivering in this group occurred also during the first 2 h, particularly on the upper part of the chest and the upper limbs, one might suggest that these patients were also uncomfortable as a result of hypothermia. The study was not designed to separate assessment of pain from that of comfort, and therefore it is not possible to speculate how hypothermia could have influenced perception of pain. Although it is recognized that pain and cold signals might be functionally related and integrated at a central level,<sup>27</sup> it remains to be verified whether the cold stimuli could affect nociceptive afferent input disproportionately.

The postoperative circulating concentrations of cortisol, glucose, and gluconeogenic substrates, although increased after surgery in both groups, were much lower than those reported previously in a group of patients undergoing a similar type of surgery with general anesthesia.<sup>28</sup> In that investigation,<sup>28</sup> the attenuation of the stress response was greatest when a continuous spinal block technique was used, with the values being comparable to those found in the current study, thereby confirming effective deafferentation. In contrast with



previous findings,<sup>6,29</sup> circulating concentrations of cortisol were not decreased by the provision of normothermia, suggesting that epidural blockade is more effective in modulating the cortisol response than the provision of normothermia.

Based on our experience with intraoperative hypothermia during general anesthesia, in which the loss of body heat causes a marked postoperative increase in catecholamines and energy expenditure, we believe that the current findings suggest that epidural local anesthetic agents attenuate significantly the metabolic response associated with moderate hypothermia. During an effective epidural nociceptive block, there was metabolic stability, even in the presence of an inadvertent decrease in body temperature.

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