Anesthesiology
74:1029–1034, 1991

Changes in Human Plasma Catecholamine Concentrations during Epidural Anesthesia Depend on the Level of Block

Rom A. Stevens, M.D., James D. Artuso, M.D.,* Tzu-Cheg Kao, Ph.D.,† Jack G. Bray, M.D.,* Loren Spitzer, C.R.N.A.,‡ David L. Louwsma, D.O.**

To test the hypothesis that increasing levels of epidural analgesia will produce progressive decreases in circulating catecholamines, we sequentially produced three levels of analgesia, T8, T4, and C8, to pin prick in young, healthy volunteers. Three percent chloroprocaine (plain) was used as the local anesthetic. The epidural analgesia was allowed to dissipate following the T8 and T4 levels of block. After the C8 level the block was reinforced to study the effect of a "top-up" dose. Blood samples were drawn from a central venous catheter. Plasma concentrations of norepinephrine and epinephrine were determined by the single isotope radioenzymatic method. Despite extensive block, hemodynamic alterations were minimal, and no significant decrease in plasma epinephrine was observed as the level of analgesia was raised to the C8 dermatome. When the level of analgesia was raised above T8, there was a trend for norepinephrine to decrease, but this decrease did not become statistically significant until analgesia reached the C8 dermatome. Reinforcing the epidural block at the C8 level of analgesia resulted an insignificant decrease in epinephrine and norepinephrine NE. Under the conditions of the present study, epidural block with a sensory analgesia level as high as C8 did not significantly decrease the plasma concentration of epinephrine in unstressed volunteers. The plasma concentration of norepinephrine significantly decreased only when the level of sensory analgesia was approximately C8. (Key words: Anesthesia techniques: epidural. Anesthetics, local: chloroprocaine. Hemodynamic response: level of epidural block. Sympathetic nervous system, catecholamines: epinephrine; norepinephrine.)

EPIDURAL ANESTHESIA causes decreased transmission in sympathetic preganglionic fibers and therefore would presumably cause a decrease in circulating catecholamine concentrations. Studies in dogs, for example, have shown that very high levels of epidural anesthesia result in a reduction in both plasma epinephrine (E) and norepinephrine (NE),[1,2] although the decrease of NE is more significant. In humans, this phenomenon has not been extensively studied. Engquist *et al.* found a moderate decrease in both E and NE in patients with a T4 level of epidural anesthesia combined with general anesthesia.[3] However, they studied only one level of block, and the induction of general anesthesia may have contributed to the decline in catecholamine concentrations. Ecoffey *et al.*[4] also found a decrease in NE but not in E in elderly men receiving epidural anesthesia, but the level of epidural block in these patients ranged from T4 to T10. There is evidence that a high level of spinal anesthesia results in a more profound decrease in catecholamines than does a low level of block,[5] but there have been no comparative studies on the effects of spinal *versus* epidural anesthesia on circulating catecholamines. Thus, it is not possible to determine, based on the available literature, what the effect of level of epidural anesthesia has on circulating plasma catecholamine concentrations.

The current study was designed to test the hypothesis that increasing levels of sensory analgesia will produce progressive decreases in circulating catecholamines. We used plasma concentrations of E and NE as an indirect measure of the effect of epidural anesthesia on the sympathetic nervous system.

Materials and Methods

After obtaining approval from our institutional review board and written informed consent from each subject, 11 anesthesiologists and nurse anesthetists were enrolled in the study. All subjects were experienced anesthesia providers between the ages of 31 and 41 yr. Three were women, and 8 were men. All were ASA physical status 1, were nonsmokers, and were taking no medications. All experiments were conducted between 7:00 AM and 3:00 PM after an overnight fast. Subjects were supine on a well-padded hospital bed during the study. Local anesthesia for insertion of central venous pressure (CVP) and epidural catheters consisted of 3 ml of *p*H-adjusted 0.5% lidocaine hydrochloride. A CVP catheter was inserted *via* an antecubital vein and advanced into the right atrium using electrocardiographic (ECG) waveform analysis. With the subject in the lateral decubitus position, an 18-G Tuohy needle was inserted into the epidural space with the bevel cephalad *via* midline approach at the second lumbar interspace and using the loss of resistance to air technique. A 20-G catheter was then inserted 5 cm into the epidural space; the needle was removed; and the patient was turned supine.

* Assistant Professor of Anesthesiology.
† Assistant Professor of Preventive Medicine (Biostatistics).
‡ Staff Nurse Anesthetist.

Received from the Departments of Anesthesiology and Preventive Medicine, The Uniformed Services University of the Health Sciences, Bethesda, Maryland and the Hospital for Special Surgery, Cornell University Medical Center, New York, New York. Accepted for publication February 25, 1991. Supported by HSETC grant 89-06-1014. Presented in abstract form at the ASA Annual Meeting, Las Vegas, Nevada, 1990.

The views presented in this article represent those of the authors and do not represent official policy of the Navy Medical Department or of the Department of Defense.

Address reprint requests to Dr. Stevens: Department of Anesthesia, The Hospital for Special Surgery, 535-E. 70th Street, New York, New York 10021.

MONITORING

The following parameters were measured: ECG and CVP (continuously); respiratory rate (RR), blood pressure (BP), and level of sensory block (every 10 min during the study). Heart rate (HR) (from the ECG) and CVP (by a pressure transducer) were measured using a Hewlett-Packard monitor (model 78342A). BPs were measured by an automated BP cuff (Dinamap, Critikon Corp., Tampa, FL). Level of sensory analgesia (absence of a sharp sensation) was determined by pin prick using a safety pin. After establishing a sharp sensation by testing over the shoulder (C4 dermatome), the pin was moved along trunk in a cephalad direction from anesthetized to unanesthetized dermatomes until the pin again felt sharp. Level of analgesia was tested bilaterally. If there was a difference between sides, the most caudad level was used.

EXPERIMENTAL PROTOCOL

After catheters were inserted, a 20-min equilibration period was used to allow the subjects to relax. The experiment was designed to produce three sequential levels of analgesia to pin prick; the levels sought were T8, T4, and C8, in ascending order. The effects of epidural anesthesia were allowed to dissipate completely prior to the next injection, except at the C8 level of block, when the effect of reinforcement of the block was studied. Each epidural injection was begun with aspiration of the catheter followed by a 3-ml test dose of 3% chloroprocaine (Nesacaine-MPF, Astra Pharmaceuticals, Westborough, MA). If no CSF was aspirated and no signs of intravascular injection seen after 1 min, the rest of the local anesthetic was given over 5–10 min. For the first injection, 15 ml of chloroprocaine was injected to achieve approximately a T8 level of analgesia. For the second injection, 25 ml was injected, to reach approximately a T4 level. For the third injection, 35 ml was injected, to reach at least a C8 level of analgesia. If the target level was not reached, an additional 5–10 ml of local anesthetic was given. Twenty min after achieving the C8 level, a final injection of 17–20 ml was injected (one half the volume of local anesthetic needed to reach a C8 level). The block levels reported are those at the time of blood sampling (*vide infra*). Between injections (except as noted above), the epidural block was allowed to dissipate completely as demonstrated by complete return of sharp sensation upon testing with a safety pin and complete return of cold sensation upon testing with an alcohol wipe.

Each subject received a slow infusion of lactated Ringer's solution but did not receive a bolus of crystalloid prior to epidural anesthesia. Whole blood drawn for catecholamine analysis was replaced with lactated Ringer's solution 3:1. Bradycardia accompanied by symptoms of nausea or malaise was treated with intravenous atropine.

Whole blood for catecholamine measurements (10 ml per sample) was drawn from the central venous catheter (over 30 s) at the following times: 1) 20 min after catheter placement, 2) 20 min after reaching approximately a T8 level of analgesia, 3) 20 min after complete dissipation of block, 4) 20 min after reaching approximately a T4 analgetic level, 5) 20 min after complete dissipation of block, 6) 20 min after reaching a C8 level of analgesia, 7) 20 min after reinjection at the C8 level of block, and 8) 20 min after dissipation of the final block.

At the end of the experiment, *i.e.*, after the last block had dissipated, subjects received epidural fentanyl 100–200 μg upon request for relief of back pain.

CONTROLS

Five of the subjects were randomly chosen as controls in a crossover design. On a different day, after an overnight fast, they underwent CVP catheter placement and rested in bed for 6 h. Blood for plasma catecholamine analysis was drawn 1) 20 min, 2) 140 min, 3) 280 min, and 4) 360 minutes after CVP catheter placement.

MEASUREMENTS OF PLASMA CATECHOLAMINES

Whole blood was drawn into heparinized syringes, cooled on ice for 10 min, and then centrifuged for 10 min at 2,000 rpm. Plasma was frozen and stored at −70° C until assay. The catecholamine assay was performed using the single isotope radioenzymatic method[6] with a lower limit of sensitivity of 10 pg/ml for NE and E. Specificity of this assay is greater than 0.98.

DATA ANALYSIS

Means ± standard errors of the means (SEM) were calculated for each variable (NE, E, systolic blood pressure [SBP], mean arterial pressure [MAP], diastolic blood pressure [DBP], HR, RR, and CVP), and analgesic level at each of the eight sampling points. Variables at each sampling point were compared to baseline measurements for each subject. Repeated-measures analysis was used to test whether there was any effect of time on the variables measured in the control group. We then tested the data for any effect of epidural anesthesia on each variable in the treatment group (*i.e.*, any effect of epidural anesthesia at the T8, T4, C8, and C8 [reinforcement] levels). If there was a statistically significant effect of either time or epidural anesthesia, we made comparisons with the baseline values for each variable. We also tested to see if there was a significant linear trend as the level of epidural anesthesia was raised. SAS GLM software was used (SAS Institute, Cary, NC). Statistical significance was assumed at $P < 0.05$.

TABLE 1. Physiologic Variables of Control Subjects

	Sample			
	1	2	3	4
E (ng/l)	63.0 ± 6.8	52.0 ± 10.8	73.2 ± 20.8	86.4 ± 5.7
NE (ng/l)	226.6 ± 32.9	257.8 ± 69.1	225.4 ± 17.9	239.2 ± 22.9
SBP (mmHg)	114.8 ± 4.8	113.6 ± 4.8	114.8 ± 4.6	117.6 ± 4.7
MAP (mmHg)	82.6 ± 2.5	81.6 ± 3.1	85.0 ± 3.9	87.0 ± 3.7
DBP (mmHg)	63.2 ± 1.4	63.0 ± 3.7	63.6 ± 3.2	67.8 ± 4.3
CVP (mmHg)	1.8 ± 1.1	2.0 ± 0.9	0.2 ± 1.0	1.8 ± 1.0
HR (min^{-1})	57.8 ± 3.4	57.6 ± 4.7	56.4 ± 4.2	60.6 ± 4.5
RR (min^{-1})	14.8 ± 0.5	14.6 ± 0.8	14.4 ± 0.8	15.6 ± 0.4

Values are mean ± SEM; n = 5.
Sample 1 drawn 20 min after CVP catheter inserted. Sample 2 drawn 120 min later. Sample 3 drawn 240 min later. Sample 4 drawn 360 min later.
There were no statistically significant differences from baseline (sample 1).
See Materials and Methods section for abbreviations.

Results

Demographic Data of the Subjects

The mean age of the subjects was 33.8 yr (range 31–41 yr). Their mean height was 177.4 cm (range 164–188 cm). Their mean weight was 73.3 kg (range 53.2–93.2 kg).

Control Subjects

There were no significant differences in age (mean 33.4, range 31–41 yr), height (mean 175.4, range 164–185 cm), or weight (mean 75.2, range 54.5–88.6 kg) between the experimental group and the control group. In the control subjects lying in bed for 6 h, there were no significant changes over time in any hemodynamic variables.

Lying in bed over 6 h without epidural anesthesia had no significant effect on either plasma NE or E (table 1).

Level of Epidural Analgesia Attained

After the first injection the mean analgesic level ± SEM was T8.1 ± 0.57. After the second injection the mean level was T4.4 ± 0.56, after the third injection C7.4 ± 0.27, and after the fourth injection (supplemental) C7.2 ± 0.29. (Note: Decimal values indicate fractions of the distance between two levels, with T4.5 halfway between T4 and T5.) There was no significant difference between right- and left-sided analgesic levels. These levels of sensory analgesia were present at the time blood samples 2, 4, 6, and 7, respectively, were drawn.

Hemodynamic Changes in Response to Epidural Anesthesia

There was no statistically significant effect of epidural anesthesia compared to resting baseline values on HR, RR, or DBP at any of the various sampling points. During epidural anesthesia, there was a decreasing trend in BP with increasing block levels. MAP decreased at the T8 level by 5%, at the T4 level by 9%, and at the C8 level by 11%, and after the C8 reinforcement by 17%, compared to baseline values. However, none of these changes was statistically significant. CVP decreased significantly from baseline measurements when the epidural block reached the T8 level ($P = 0.004$), and there was a significant decrease as the block was raised ($P = 0.0001$) (fig. 1). After epidural anesthesia, we found that only SBP (+12%, $P = 0.03$)) and MAP (+12%, $P = 0.013$) significantly increased compared to baseline values, but only after final block had dissipated. This latter increase in BP occurred at a time when all of the subjects were complaining of lower back pain (*vide infra*) (table 2).

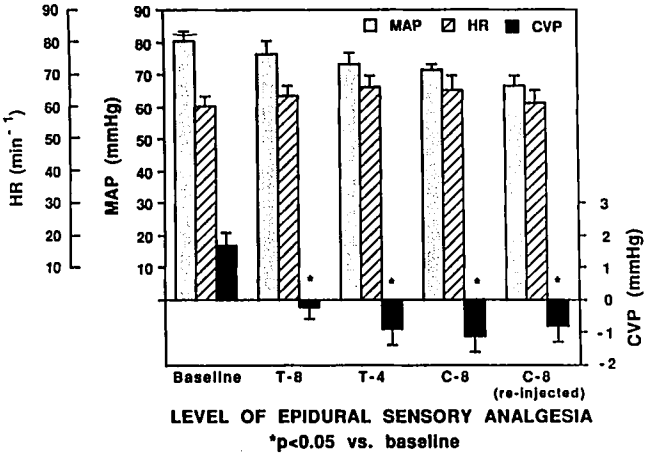

FIG. 1. Hemodynamic variables (n = 10), means ± SEM for three levels of epidural block, with a "top-up" at the C8 level of analgesia, compared to resting baseline values. These variables were recorded at the time of blood sampling for catecholamine analysis. Heart rate (HR), mean arterial pressure (MAP), and central venous pressure (CVP) are shown as a function of dermatome level of EA. There were no significant changes, except a decrease in CVP at all levels of block were seen. There was no significant effect of reinjection of the epidural catheter when the block was at the C8 level.

TABLE 2. Physiologic Variables of Subjects Receiving Epidural Anesthesia

	Sample							
	1	2	3	4	5	6	7	8
E (ng/l)	64.1 ± 15.2	53.1 ± 19.6	78.9 ± 12.2	72.2 ± 14.7	81.8 ± 21.4	42.0 ± 11.6	38.2 ± 7.2	89.2 ± 17.7
NE (ng/l)	195.3 ± 34.5	195.0 ± 45.3	261.7 ± 23.8	143.9 ± 29.1	240.4 ± 43.6	105.3 ± 26.2*	80.6 ± 21.1*	282.5 ± 47.9
SBP (mmHg)	109.2 ± 3.9	106.6 ± 5.5	112.0 ± 4.3	102.4 ± 4.2	117.7 ± 3.4	100.4 ± 4.5	95.7 ± 5.3	122.1 ± 3.8*
MAP (mmHg)	80.3 ± 3.0	76.3 ± 4.2	83.1 ± 4.1	73.2 ± 3.4	87.3 ± 2.6	71.2 ± 2.1	66.6 ± 3.0	89.9 ± 2.4*
DBP (mmHg)	64.5 ± 3.2	60.5 ± 3.3	66.7 ± 4.0	56.5 ± 2.9	67.6 ± 2.4	53.7 ± 1.7	50.4 ± 2.1	70.5 ± 2.5
CVP (mmHg)	1.7 ± 0.4	−0.2 ± 0.4*	2.3 ± 0.8	−0.9 ± 0.5*	1.8 ± 0.3	−1.1 ± 0.5*	−0.8 ± 0.5*	2.4 ± 0.8
HR (min^{-1})	60.4 ± 2.9	63.5 ± 3.0	60.4 ± 3.0	66.1 ± 3.5	64.7 ± 4.0	65.4 ± 4.4	61.4 ± 3.8	73.4 ± 4.7
RR (min^{-1})	13.9 ± 0.4	14.6 ± 0.5	14.4 ± 0.8	14.8 ± 0.9	14.8 ± 0.3	13.8 ± 0.8	15.0 ± 0.9	17.2 ± 0.9

Values are mean ± SEM; n = 10.
Sample 1 (baseline) drawn 20 min after epidural and CVP catheters inserted. Sample 2 drawn 20 min after achieving a T8 level of sensory analgesia. Sample 3 drawn 20 min after dissipation of T8 block. Sample 4 drawn 20 min after achieving a T4 level of sensory analgesia. Sample 5 drawn 20 min after dissipation of T4 block. Sample 6 drawn 20 min after achieving a C8 level of sensory analgesia. Sample 7 drawn 20 min after re-injection of epidural catheter at C8 level of analgesia. Sample 8 drawn 20 min after complete dissipation of final epidural block.
See Materials and Methods section for abbreviations.
* $P < 0.05$ *versus* baseline (sample 1).

Effect of Epidural Anesthesia upon Plasma NE and E Concentrations

Plasma E concentration (mean ± SEM) was 64 ± 15 ng/l in the baseline state. There was no statistically significant change from the baseline resting state in E concentration at any level of analgesia. Although there was a decreasing trend in E as the level of analgesia was raised to C8 (−34% *vs.* baseline) and after the C8 "top-up" dose (−40% *vs.* baseline), this trend was not statistically significant ($P = 0.124$).

Plasma NE concentration (mean ± SEM) was 195 ± 34 ng/l in the baseline state. There was no significant change at the T8 level of analgesia from baseline. As the block was raised above the T8 level, there was a significant decreasing linear trend ($P = 0.013$); however, the absolute decrease in NE concentrations did not become statistically significant until the level of block reached the C8 dermatome (−46% *vs.* baseline). There was a small but statistically insignificant decrease in NE after reinforcement at the C8 level (−23% *vs.* C8, $P = 0.078$) (fig. 2).

Plasma NE and E concentrations measured after each block had dissipated (*i.e.*, sampling points 3, 5, and 8) were not statistically different from baseline values, despite moderate to severe back pain noted by all subjects after the final epidural block had dissipated (table 2, sampling point 8).

Complications

Two subjects developed bradycardia (HR < 50 beats per min) and hypotension (SBP < 80 mmHg) accompanied by nausea and malaise. These episodes resolved after intravenous atropine (0.4 mg). In both instances this occurred at least 20 min prior to catecholamine sampling. In both instances, bradycardia was observed when the block level was T4 or below. One subject developed an acute onset of atrial fibrillation with a rapid ventricular rate. He was treated initially with intravenous verapamil and esmolol and later with oral propranolol. On the next day, still in atrial fibrillation, his cardiac rhythm converted to sinus after intravenous procainamide. This episode occurred just after the second injection, and the subject's data were not included in the analysis.

By the end of the study, after epidural analgesia had dissipated, all subjects reported moderate to very severe lumbar back pain. This was relieved by epidural fentanyl 100–200 μg and with oral ibuprofen 800 mg, and the pain did not return. No back pain was reported by any of the control subjects lying in bed without epidural anesthesia.

Discussion

Since the adrenal medulla is innervated by sympathetic fibers originating from the T6 to L2 spinal segments,[7] we

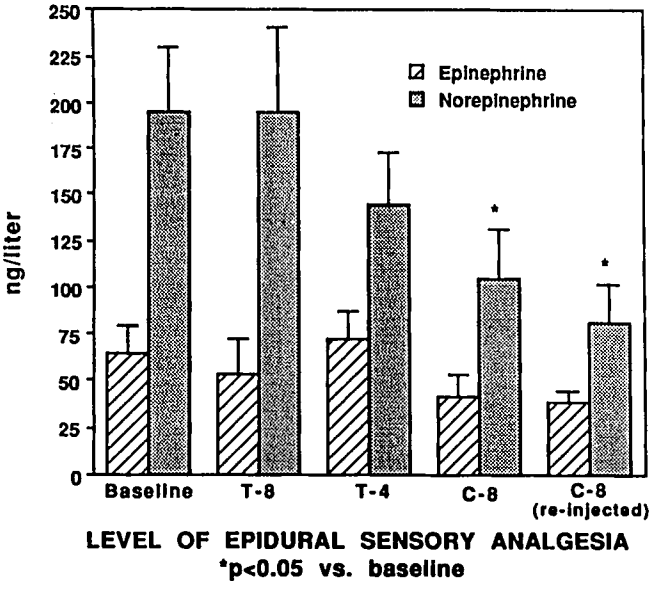

FIG. 2. Plasma catecholamine concentrations during EA compared to resting baseline values (n = 10), means ± SEM for three levels of epidural analgesia and a supplemental dose at the C8 level. No statistically significant change in E was detected. Above the T8 dermatome, there was a significant downward trend in NE as the block level was raised, but the absolute decrease in NE concentration did not become significant until the block reached the C8 level. There was no significant effect of reinjection at the C8 level upon either NE or E.

expected to see a decrease in plasma E concentrations when we achieved sensory analgesia of those dermatomes. However, we observed no significant change in plasma E at any level of analgesia studied. On the other hand, we expected to see the observed decrease in circulating plasma NE concentrations as a progressively greater proportion of the sympathetic nerve terminals in the periphery became blocked by raising the level of epidural anesthesia. Apparently, when the epidural sensory level is at T4 and below, NE release from unblocked segments in young fit subjects is adequate to compensate for a decrease in NE release in segments below the level of analgesia. As more spinal segments are blocked, this compensatory mechanism fails, and plasma NE begins to decline. Since epidural anesthesia is assumed to produce a complete sympathectomy, it is surprising that even with a C8 level of sensory analgesia, plasma concentration of NE persisted at about 50% of baseline values. This observation supports Bromage's view that neural blockade with local anesthetics results in merely a reduction, rather than in a complete interruption of neural traffic.[8]

Despite extensive epidural analgesia, we saw only small decreases in BP compared to baseline in these young, healthy volunteers, who had not received bolus administration of intravenous fluid prior to epidural block. In a study of volunteers by Bonica *et al.*,[9] lidocaine lumbar epidural anesthesia to T4 produced a 15% decrease in total peripheral resistance, concomitant with a 23% increase in cardiac output, resulting in a 5% decrease in MAP. When the level of block was raised to T1 by injecting additional lidocaine *via* a thoracic epidural catheter, total peripheral resistance decreased 19% compared to control values, with cardiac output remaining at baseline levels, resulting in a 16% decrease in MAP. They also observed a rise in CVP at this high level of block. Except for this latter observation, Bonica's observations were very similar to those of the current study.

The volunteers in Bonica's study[9] had very high plasma concentrations of lidocaine (4–7 μg/ml). He suggested that these plasma lidocaine concentrations were responsible for cardiac stimulation, offsetting the vasodilating effects of a high sympathetic block. In our study, presumably any hemodynamic effects of the local anesthetic had dissipated by the time our measurements were made because of the rapid metabolism of chloroprocaine in the plasma. The high plasma lidocaine concentrations in Bonica's subjects may account for the increase in CVP he observed, whereas our subjects demonstrated a decrease in CVP. Thus, factors other than sympathetic blockade may influence hemodynamic changes seen during epidural anesthesia.

Why neither we nor Bonica[9] observed a marked decrease in BP despite a very high epidural block is unclear. We suspect that the sympathectomy produced by even very high levels of epidural anesthesia is not complete compared to that produced by a spinal anesthetic of the same extent (*vide infra*). This view is supported by the minimal changes in plasma catecholamine concentrations observed in the current study. Another possibility is that other hormonal systems intervene to support the BP. For example, Peters *et al.*[10] have shown in an awake canine epidural model that plasma vasopressin increases dramatically in dogs with very high lumbar epidural anesthesia. BPs were well maintained in these dogs. When a vasopressin antagonist was given, BP decreased precipitously. Circulating catecholamine concentrations were well maintained in these dogs despite an extensive epidural block.[11] It is not known whether similar changes in plasma vasopressin occur in humans undergoing epidural anesthesia.

Our observations of catecholamines concentrations during epidural anesthesia agree with those of Ecoffey *et al.*,[4] who studied elderly men with 0.5% bupivacaine epidural anesthesia. They found a slight decrease in NE but not in E in patients with blocks ranging from T4 to T10. However, Ecoffey's group was not able to relate the level of neural blockade with changes in NE. Further, their study population consisted of elderly men (mean age 72 yr), who had higher baseline concentrations of catecholamines than did our younger subjects, indicating a higher resting sympathetic tone. A difference in plasma cate-

cholamine concentrations between young and old subjects has been reported previously.[12]

The results of the current study differ somewhat from those seen in patients under spinal anesthesia. Pflug and Halter reported a linear relationship between the height of hyperbaric tetracaine spinal anesthesia and both NE and E plasma levels.[5] They concluded that spinal anesthesia had a depressant effect on adrenergic tone dependent upon the dermatome level of block, with a marked decrease in both NE and E when the block level was T6 or higher. In contrast, when the block level was below T9, there was very little change in plasma catecholamine levels. The decrease in E concentrations seen under spinal but not epidural anesthesia may be explained by a more complete neural blockade of the efferent sympathetic innervation of the adrenal medulla.

Lundin *et al.* used intraneural recordings to measure (peripheral) muscle sympathetic activity during 2% lidocaine epidural anesthesia in human volunteers.[13] They found that sensory epidural analgesia above T10 effectively blocked spontaneous and evoked muscle sympathetic activity in the peroneal nerve. Epidural anesthesia appears to result in a profound decrease in neural traffic in the sympathetic innervation of the periphery, but it has a lesser effect on the innervation of the adrenal medulla. This could explain why we[1] and other authors[4,11,14] in experiments both in dogs and in humans, have found that epidural anesthesia results in a significant decrease in the circulating concentration of NE but little change in E. However, to evaluate this hypothesis, one would have to directly measure neural traffic in sympathetic efferents to the adrenal medulla.

In summary, during epidural anesthesia with 3% chloroprocaine in resting and unstressed human volunteers with epidural blocks to C8, we observed no significant change in plasma E concentrations. Raising sensory neural blockade above the T8 dermatome tended to lower plasma concentrations of NE, but this did not become statistically significant until a C8 level of analgesia was reached. Reinforcing the epidural blockade at the C8 level did not significantly affect the plasma concentrations of E or NE. If circulating plasma catecholamine concentrations are an indicator of sympathetic function, these results suggest that epidural anesthesia with 3% chloroprocaine (plain) produces only a partial sympathectomy even at high levels of sensory analgesia.

The authors wish to thank Professor Philip Bromage, Professor Kamran Samii, and Dr. Nigel Sharrock for their kind review of this manuscript. They also wish to acknowledge the dedication of the volunteers of this study, many of whom are now serving with United States Naval forces in the Persian Gulf.

References

1. Stevens RA, Lineberry PJ, Arcario TJ, Bacon GS, Cress LW: Epidural anaesthesia attenuates the catecholamine response to hypoventilation in dogs. Can J Anaesth 37:867–872, 1990
2. Stevens RA, Schubert A, Mikat-Stevens M, van Clief M: Epidural anesthesia significantly reduces resting plasma catecholamine levels in awake dogs (abstract). ANESTHESIOLOGY 69:A337, 1988
3. Engquist A, Fog-Moeller F, Christiansen C, Thode J, Vester-Andersen T, Nistrup-Madsen S: Influence of epidural anesthesia on the catecholamine and cyclic AMP responses to surgery. Acta Anaesthesiol Scand 24:17–21, 1980
4. Ecoffey C, Edouard A, Pruszczynski W, Taly E, Samii K: Effects of epidural anesthesia on catecholamines, renin activity, and vasopressin changes induced by tilt in elderly men. ANESTHESIOLOGY 62:294–297, 1985
5. Pflug AE, Halter JB: Effect of spinal anesthesia on adrenergic tone and the neuroendocrine responses to surgical stress in humans. ANESTHESIOLOGY 55:120–126, 1981
6. Peuler JD, Johnson GA: Simultaneous single isotope radioenzymatic assay of plasma norepinephrine, epinephrine, and dopamine. Life Sci 21:626–636, 1977
7. Bonica JJ: Autonomic innervation of the viscera in relation to nerve block. ANESTHESIOLOGY 29:793–813, 1968
8. Bromage PR: Epidural Analgesia. Philadelphia, WB Saunders, 1978, pp 350–351, 357–365
9. Bonica JJ, Berges PU, Morikawa K: Circulatory effects of peridural block: I. Effects of level of analgesia and dose of lidocaine. ANESTHESIOLOGY 33:619–626, 1970
10. Peters J, Schlaghecke R, Thouet H, Arndt JO: Endogenous vasopressin supports blood pressure and prevents severe hypotension in conscious dogs. ANESTHESIOLOGY 73:694–702, 1990
11. Peters J, Kutkuhn B, Medert HA, Schlaghecke R, Schuettler J, Arndt JO: Sympathetic blockade by epidural anesthesia attenuates the cardiovascular response to severe hypoxemia. ANESTHESIOLOGY 72:134–144, 1990
12. Ziegler MG, Lake CR, Kopin IJ: Plasma noradrenalin increases with age. Nature 261:333–335, 1976
13. Lundin S, Wallin G, Elam M: Intraneural recording of muscle sympathetic activity during epidural anesthesia in humans. Anesth Analg 69:788–93, 1989
14. Stanek B, Schwarz M, Zimpfer M, Raberger G: Plasma concentrations of noradrenalin and adrenalin and plasma renin activity during extradural blockade in dogs. Br J Anaesth 52:305–310, 1980.