Hemodynamic Effects of Dopamine during Thoracic Epidural Analgesia in Man

Johan Lundberg, M.D.,* Lars Norgren, M.D., Ph.D.,† Dick Thomson, M.D., Ph.D.,‡ Olof Werner, M.D., Ph.D.§

The cardiovascular effects of dopamine were studied before and during thoracic epidural analgesia (TEA) in eight patients prior to abdominal aortic surgery. Dopamine was infused at rates of 2, 4, and 8 $\mu g \cdot kg^{-1} \cdot min^{-1}$. Mean plasma dopamine concentration increased proportionally to the infusion rate. Before TEA, dopamine 8 $\mu g \cdot kg^{-1} \cdot min^{-1}$ decreased systemic vascular resistance 4 ± 4 mmHg min $\cdot l^{-1}$ (m ± SD) ($P < 0.05$), but increased mean arterial pressure 15 ± 12 mmHg ($P < 0.01$), cardiac output 1.9 ± 1.0 l · min^{-1} ($P < 0.01$), heart rate 10 ± 9 beats · min^{-1} ($P < 0.05$), and plasma norepinephrine concentration 544 ± 252 pg · ml^{-1} ($P < 0.01$). After the induction of TEA, which extended above the T2 dermatome and below the L2 dermatome, saline and albumin were infused to maintain central venous and pulmonary capillary wedge pressures. TEA reduced mean arterial pressure from 96 ± 18 to 55 ± 8 mmHg ($P < 0.01$), cardiac output from 4.7 ± 0.9 to 3.9 ± 0.9 l · min^{-1} ($P = 0.05$), systemic vascular resistance from 21 ± 6 to 14 ± 3 mmHg min · l^{-1} ($P < 0.05$), and plasma norepinephrine concentration from 394 ± 141 to 207 ± 73 pg · ml^{-1} ($P < 0.01$). The plasma epinephrine concentration was reduced 49% after the induction of TEA. During TEA, dopamine, 8 $\mu g \cdot kg^{-1} \cdot min^{-1}$ increased mean arterial pressure by 57 ± 9 mmHg ($P < 0.01$), cardiac output by 2.9 ± 0.8 l · min^{-1} ($P < 0.01$), heart rate by 14 ± 11 beats · min^{-1} ($P < 0.01$), and plasma norepinephrine concentration by 833 ± 499 pg · ml^{-1} ($P < 0.01$). Systemic vascular resistance changed in a diphasic fashion. Thus, at 2 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of dopamine, the value decreased further, below the level seen with TEA alone, but increased at 4 and 8 $\mu g \cdot kg^{-1} \cdot min^{-1}$. In addition, at 8 $\mu g \cdot kg^{-1} \cdot min^{-1}$, mean pulmonary artery pressure and pulmonary capillary wedge pressure were greater during than before TEA, although the values were similar without dopamine. The authors conclude that the effects of dopamine on mean arterial pressure, cardiac output, systemic vascular resistance, pulmonary capillary wedge, and mean pulmonary artery pressure were different during TEA, as compared to before the block. A moderate dose of dopamine (4 $\mu g \cdot kg^{-1} \cdot min^{-1}$) was sufficient to maintain mean arterial pressure and cardiac output at adequate levels during TEA although systemic vascular resistance remained low. (Key words: Anesthetics, local: mepivacaine. Anesthetic techniques: thoracic epidural. Dopamine: cardiovascular effects. Sympathetic nervous system, catecholamines: dopamine; epinephrine; norepinephrine.)

THORACIC EPIDURAL ANALGESIA (TEA) is usually accompanied by a decrease in arterial pressure due to a blockade of sympathetic nerves, especially if the cardiac innervation is involved.[1-4] Several sympathomimetic drugs, e.g., isoproterenol,[2,5] norepinephrine,[2] ephedrine,[6] and prenalterol,[4] have been used to counteract the hypotension. The use of dopamine to treat the hypotension might have certain advantages related to its dose-dependent hemodynamic effects. Dopamine mainly activates beta-1 and dopamine receptors at infusion rates below 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$, while stimulation of alpha receptors becomes prominent at higher infusion rates.[7,8] Because of its short onset and plasma half-life, the cardiovascular effects of dopamine are easily controlled by changing the infusion rate.[9] It is, therefore, our practice to use dopamine infusion to maintain arterial pressure during TEA if normotension cannot be maintained by volume loading alone. Previous reports on the use of dopamine during regional analgesia in man demonstrate that dopamine maintains arterial pressure during spinal anesthesia for caesarean section[10] and during TEA.[11] However, dose-effect studies have not been made. We studied plasma catecholamine concentrations and hemodynamics while dopamine was infused at stepwise increased rates before and during TEA in patients scheduled for abdominal aortic reconstructive surgery.

Methods and Materials

The study was approved by the local Human Investigations Committee and informed consent was obtained. Eight patients of either sex were studied prior to surgery. The age was 64 ± 12 yr (mean ± 1 SD) and the weight was 62 ± 8 kg. All patients belonged to ASA p.s. II. The reason for surgery was either obliterative vascular disease (n = 2) or abdominal aortic aneurysm (n = 6). One patient had been treated for an uncomplicated myocardial infarction 3 yr previously, and another patient suffered from bronchitis. No patient had signs of severe lower limb ischemia or cardiac failure at rest. One patient was receiving digoxin, but none used beta-adrenergic blocking drugs or calcium antagonists. Morphine hydrochloride 5–10 mg was given IM 30 min before arriving in the operating room. Additional 2 mg increments were given iv during the investigation if further sedation was needed. An epidural catheter (Portex®) was introduced 2–3 cm into the epidural space with a median approach through the T7-T8 or T8-T9 interspaces. A balloon-tipped flow directed triple lumen thermal dilution catheter (IL 44166, 7F) was inserted under local anesthesia through the right jugular vein to an adequate position in the pulmonary artery.

TABLE 1. Outcome of Three-way Analysis of Variance for Hemodynamics and Plasma Catecholamines. The *P*-value is Shown

	HR	MAP	CO	SVR	CVP	PCWP	MPAP	PVR	Norepinephrine	Epinephrine
Interaction TEA-dopamine	n.s.	<0.001	0.017	<0.001	n.s.	<0.001	<0.001	n.s.	0.007	n.s.
Main effects										
TEA	<0.001	–	–	–	<0.001	–	–	n.s.	–	<0.001
Dopamine	<0.001	–	–	–	<0.001	–	–	0.044	–	n.s.

n.s. = not significant (*P* > 0.05); – = the *P*-value is not shown since significant interaction TEA-dopamine was present.

Cardiac output (CO) was determined by thermodilution (IL 701, Cardiac Output Computer, Instrumentation Laboratories) as the mean of three consecutive measurements. Iced 5.5% dextrose was utilized as thermal indicator, administered with a pump injector at end expiration. A radial artery cannula was inserted and pulmonary arterial and central venous pressures were obtained with Hewlett & Packard pressure transducers (HP 1280 C). An ECG lead (V_5), mean arterial pressure (MAP), mean pulmonary artery pressure (MPAP), and central venous pressure (CVP) were continuously recorded on a Mingograph-81 (Elema-Schönander, Sweden). Pulmonary capillary wedge pressure (PCWP) was obtained intermittently by inflating the balloon. Both the unfiltered pressure curves and damped curves representing mean pressure were recorded.[12] Systemic vascular resistance (SVR) was calculated as (MAP-CVP)/CO and pulmonary vascular resistance (PVR) was obtained as (MPAP-PCWP)/CO.

After insertion of the catheters, the patient rested for 15 min before a first set of measurements were taken. Dopamine (Intropin®, Arnar-Stone), 100 mg in 500 ml dextrose 5.5%, was then administered iv at a rate of 2, 4, and 8 $\mu g \cdot kg^{-1} \cdot min^{-1}$ with an infusion pump. The infusion was continued for 10 min at each rate. Since a steady state plasma dopamine level is almost reached after 5 min,[9] measurements were made during the final 5 min. Arterial plasma catecholamine samples were drawn no earlier than 6 min after the start of the infusion. A control measurement was obtained 12 min after stopping the dopamine infusion.

To establish TEA, 6–10 ml mepivacaine 20 mg · ml^{-1} (Carbocain®, Astra) was injected *via* the epidural catheter. A continuous infusion of mepivacaine 20 mg · ml^{-1} at 7–10 ml · h^{-1} was started 30 min later. The distribution of sensory loss was determined by pin-prick and with chlorethylene cooling spray. In each patient the upper limit of the sensory block was above the second thoracic dermatome. The lower limit was below the second lumbar dermatome. Hemodynamic data were obtained 25–40 min after the mepivacaine injection. Arterial samples for plasma mepivacaine estimation were taken in five patients. While TEA was established, each patient received 500 ml

5% albumin solution and approximately 1000 ml Ringer's acetate to maintain central venous pressure and pulmonary capillary wedge pressure at the same levels as during the control measurement without dopamine before TEA. Subsequently, dopamine was infused and the hemodynamic effects were recorded as outlined above, except that dopamine was not stopped in order to obtain a final control measurement. Body temperature was maintained at 36–37° C. The investigation lasted 2 h. Thereafter, surgery was performed during a combination of general anesthesia and TEA.

ANALYSES

Arterial samples for measurements of plasma dopamine, norepinephrine, and epinephrine concentrations were taken in EGTA + glutathione prepared tubes and immediately centrifuged and stored at −70° C until analyzed using high pressure liquid chromatography.[13]

Plasma dopamine, norepinephrine, and epinephrine activity were measured with an inter-assay sensitivity of 5–15%, depending on the catecholamine level in each sample. The minimum detectable level of epinephrine was 30 pg · ml^{-1}, and the reference values for norepinephrine were 170–680 pg · ml^{-1}, for epinephrine < 75 pg · ml^{-1}, and for dopamine < 60 pg · ml^{-1} with this method. Plasma mepivacaine levels in five patients were measured in arterial samples stored at −70° C until assayed at Astra AB, Södertälje, Sweden, using a gaschromatographical and masspectrometrical technique. In five patients, arterial bloodgas samples were drawn before and during TEA and analyzed with an IL 413 blood gas analyser (Instrumentation Laboratories).

STATISTICS

Three-way analysis of variance with 4 × 2 × 8 cells (dopamine dosage (4); before-during TEA (2); patients (8)) was performed to assess the significance of interaction dopamine-TEA (table 1). The significance of "main effects" was only tested if no interaction was present.[14] The analysis was finished by pairwise comparison with the *t* test if either significant interaction or a significant main effect was found. *P* < 0.05 was considered to be significant.

TABLE 2. Plasma Catecholamine Changes During Dopamine Infusion Before and During TEA

Dopamine Infusion Rate, $\mu g \cdot kg^{-1} \cdot min^{-1}$	0	2	4	8	Post-infusion Control
Plasma norepinephrine: (pg · ml⁻¹)					
Preblock	394 ± 141	421 ± 167	518 ± 185†	938 ± 346†	479 ± 165*
TEA	207 ± 73§	226 ± 68‡	367 ± 80†‡	1040 ± 474†	–
Plasma epinephrine: (pg · ml⁻¹)					
Preblock	113 ± 66	148 ± 170	140 ± 161	148 ± 99	76 ± 51
TEA	58 ± 50	72 ± 50	68 ± 58	103 ± 83	–
Plasma dopamine: (ng · ml⁻¹)					
Preblock	<0.5	37 ± 15†	75 ± 27†	139 ± 104†	8 ± 3†
TEA	0.9 ± 0.3	41 ± 12†	77 ± 38†	156 ± 97†	–

* ($p < 0.05$) and †($p < 0.01$): Significant change compared to findings before dopamine infusion.

‡ ($p < 0.05$) and §($p < 0.01$): Significant change compared to findings before TEA at the same dopamine infusion rate.

– = No postinfusion control was performed during TEA.

The values are presented as mean ± 1 SD in the text and table 2, and as mean ± 1 SEM in figure 1.

Results

The patients were awake and cooperative throughout the investigation. One patient complained of nausea, and two other patients had an increased number of extrasystoles at 8 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of dopamine, both before and during TEA. Mean values for arterial pH, P_{O_2}, P_{CO_2}, and base excess during airbreathing in five patients were 7.42 ± 0.03, 69 ± 5 mmHg, 42 ± 1 mmHg, and 2 ± 2 mM, respectively, before TEA. The corresponding figures during TEA were 7.40 ± 0.04, 75 ± 10 mmHg, 44 ± 1

FIG. 1. Changes in HR, MAP, CO, SVR, CVP, PCWP, MPAP, and PVR by dopamine before (---) and during (—) TEA. Values are mean and 1 SEM. The last point is the post-infusion control value obtained before TEA. * and **: significant differences before/during TEA ($P < 0.05$ and $P < 0.01$ respectively). ☆ and ☆☆: significant change in comparison to the measurement without dopamine.
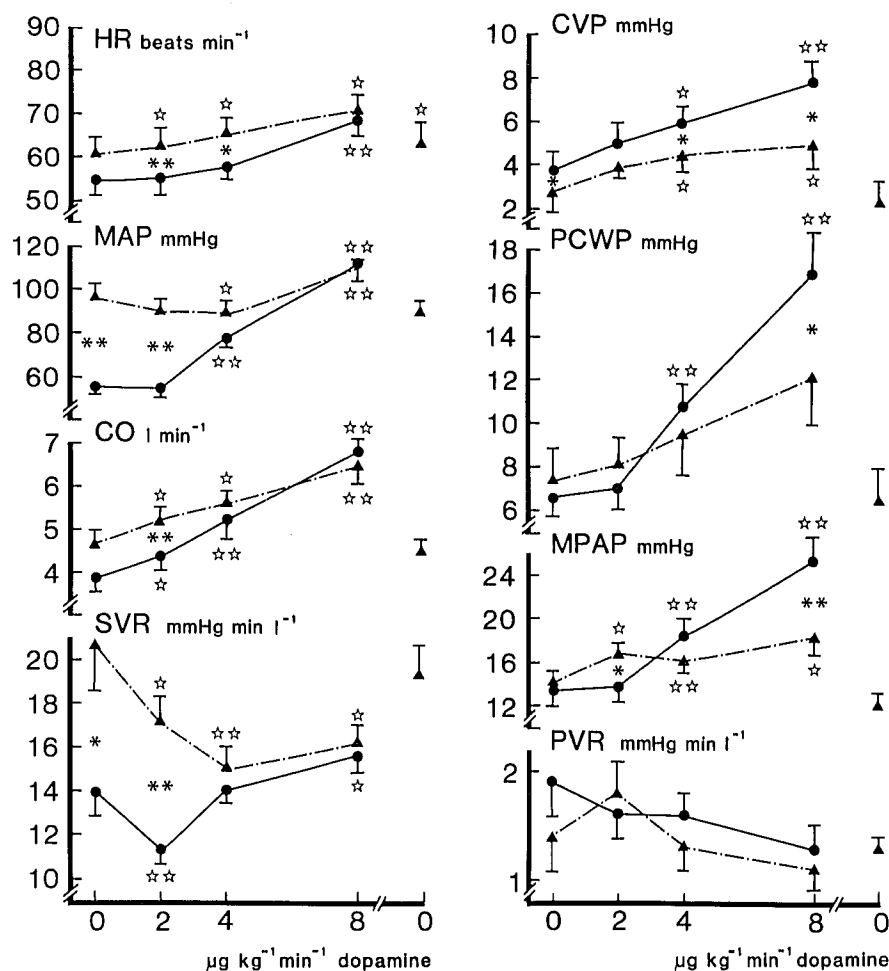
mmHg, and 1 ± 4 mM, *i.e.*, there was no significant change. During TEA the mean plasma mepivacaine concentrations in five patients were 1.7 ± 0.4, 1.5 ± 0.4, 1.5 ± 0.2, and 1.9 ± 0.2 $\mu g \cdot ml^{-1}$ at the dopamine infusion rates of 0, 2, 4, and 8 $\mu g \cdot kg^{-1} \cdot min^{-1}$, respectively. The highest individual value recorded was 2.4 $\mu g \cdot ml^{-1}$.

PLASMA CATECHOLAMINE CONCENTRATIONS

The mean value for arterial dopamine concentration increased in proportion to the infusion rate, with very similar values before and during TEA (table 2).

Before TEA, and before dopamine, arterial norepinephrine (NE) concentration was 394 ± 141 pg $\cdot ml^{-1}$ increasing to 938 ± 346 pg $\cdot ml^{-1}$ at 8 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of dopamine (table 2). The post infusion plasma NE level was slightly elevated (479 ± 165 pg $\cdot ml^{-1}$, $P < 0.05$) compared to the preinfusion level. TEA reduced NE concentration 48% when no dopamine was being administered, but the NE concentration increased more in response to dopamine during TEA so that the NE concentration at 8 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of dopamine was similar to the corresponding value obtained before TEA. The plasma epinephrine concentration was unaffected by dopamine infusion (tables 1, 2), but was significantly reduced by TEA according to the anova (table 1).

HEMODYNAMICS

Effects of dopamine before TEA. Mean values for HR, CO, CVP, and MPAP increased gradually with the dopamine infusion rate. At 8 $\mu g \cdot kg^{-1} \cdot min^{-1}$, cardiac output was 40% above the control value. Mean arterial pressure was significantly less than control at 4 $\mu g \cdot kg^{-1} \cdot min^{-1}$ ($P < 0.05$), but greater than control at 8 $\mu g \cdot kg^{-1} \cdot min^{-1}$ ($P < 0.01$). Dopamine caused a decrease in systemic vascular resistance at all these infusion rates with the lowest mean value at 4 $\mu g \cdot kg^{-1} \cdot min^{-1}$. No significant change in PCWP and PVR was found before TEA. In addition, there was no significant difference between the hemodynamic measurements at the postinfusion control and the initial measurement without dopamine, except for HR which increased by 4 beats $\cdot min^{-1}$ ($P < 0.05$) (fig. 1).

Effects of TEA. In comparison with the observations obtained before TEA without dopamine, TEA reduced mean CO by 18% ($P = 0.05$), MAP by 43% ($P < 0.01$), and SVR by 33% ($P < 0.05$). HR increased by 5 beats $\cdot min^{-1}$ in one patient and decreased by 1–23 beats $\cdot min^{-1}$ in the others (not significant). CVP increased 1 ± 1 mmHg ($P < 0.05$), while PCWP, MPAP, and PVR were unaltered (fig. 1).

Effects of dopamine during TEA. The increases in MAP, CO, PCWP, and MPAP caused by dopamine were more marked during than before TEA. This was confirmed by a statistically significant interaction between dopamine and

TEA effects (table 1). HR and CVP increased progressively with the dopamine infusion rate, but the response was not significantly different from conditions before TEA (table 1).

Two $\mu g \cdot kg^{-1} \cdot min^{-1}$ induced no significant change in MAP, but 4 $\mu g \cdot kg^{-1} \cdot min^{-1}$ caused a marked increase, in contrast to what was observed before TEA. There was a diphasic response in SVR, which decreased at 2 $\mu g \cdot kg^{-1} \cdot min^{-1}$, but increased again as the dopamine infusion rate was raised. Dopamine had no obvious effect on PVR (fig. 1).

Discussion

EFFECTS OF DOPAMINE BEFORE TEA

Plasma dopamine concentration was proportional to the infusion rate and the values found by us are consistent with previous reports.[9,15] In the present study, the samples were taken at least 6 min after each increase in infusion rate. As dopamine has a short plasma half-life, the infusion periods were adequate for plasma dopamine concentration to reach a steady state. This is supported by the findings by Järnberg *et al.*,[9] that the plasma concentration is nearly the same at 5 and 30 min of constant dopamine infusion. It is less certain that other dopamine effects also reached steady state. Thus, the same authors also found that plasma NE concentration increased continuously during the first half hour of infusion. Therefore, we were careful to standardize the times for blood sampling and hemodynamic measurements. However, it has been found in healthy volunteers that the plasma NE concentration must exceed 1800 pg $\cdot ml^{-1}$ to produce any hemodynamic and/or metabolic effects.[16] In our study, the NE levels only reached 938 ± 346 pg $\cdot ml^{-1}$ at the 8 $\mu g \cdot kg^{-1} \cdot min^{-1}$ dopamine infusion rate before TEA.

The hemodynamic findings resemble those found by others.[17,18] Thus, CO increased continuously with the increasing infusion rate, while SVR and MAP decreased at low infusion rates. The increase in CVP and PCWP may probably be attributed to alpha receptor mediated vasoconstriction of capacitance vessels.[19,20] The unchanged pulmonary vascular resistance has also been noted earlier.[21,22]

EFFECTS OF TEA

The reduced plasma NE concentration during TEA reflects the decreased sympathetic nervous activity with inhibited release of catecholamines from the sympathetic nerve fibers.[23] The circulatory effects that we observed were similar to those found by McLean *et al.*[2] after combined cervical and lumbar epidural analgesia with mepivacaine. Thus, CO, MAP, and SVR were markedly reduced. These changes occurred in spite of the fact that

CVP and PCWP were maintained by infusion of fluid. Hence, it appears that TEA reduced cardiac contractility.

The decrease in MAP during TEA was more profound than in a number of previous studies. This may be due to differences in study design. Bonica et al.[1] used rather large doses of lidocaine in young volunteers, which may have resulted in plasma concentrations high enough to cause circulatory stimulation. The plasma mepivacaine concentrations that we found (below 2.5 μg · ml^{-1}) were too small to exert any direct systemic effects which only occur at approximately 5–6 μg · ml^{-1}.[24] Otton and Wilson[3] and Ottesen[25] used rather low doses of mepivacaine which explains why the sympathetic block was probably less effective than in our investigation. In addition, these authors studied younger patients.

EFFECTS OF DOPAMINE DURING TEA

An adrenoceptor agonist may be expected to have more profound effects against a background of a reduced, instead of a normal or increased, sympathetic nervous activity. In fact the hemodynamic effects of dopamine after TEA were markedly different from those observed before TEA. Butterworth et al.,[26] who studied dogs during cardiopulmonary bypass, found evidence that dopamine causes venous constriction during, but not before, spinal anesthesia. This agrees well with the greater increases in PCWP during than before TEA in the present study (fig. 1). Another reason for the pronounced increases in PCWP, MPAP, and CVP during dopamine infusion would be the volume expansion that took place during the induction of TEA. MAP and CO increased so much during dopamine infusion that the values at 8 μg · kg^{-1} · min^{-1} were similar to those found at the same infusion rate before TEA. However, the increased PCWP suggested that left ventricular contractility was less.

At 2 μg · kg^{-1} · min^{-1} dopamine, SVR decreased below the level seen with TEA alone. Thus, dopamine caused further vasodilatation, in spite of an existing marked reduction in sympathetic tone. In this respect, our data contradict the statement by Lokhandwala and Barrett[27] that an intact sympathetic system is required to observe the initial vasodilating effects of dopamine. They suggested that the vasodilatation is mostly due to stimulation of prejunctional dopamine receptors, which inhibit transmission via vasoconstrictor fibers. Following neurogenic blockade, only an alpha receptor mediated vasoconstriction would be present.[28] Stimulation by dopamine of sympathetic nerve fibers, still intact in spite of the block,[29] could explain the previously mentioned contradiction. A more likely explanation is that dopamine caused vasodilatation directly through stimulation of postjunctional (DA-1) receptors, e.g., in the splanchnic and renal vasculature.[7] Since dopamine is a very weak beta-2 agonist,[7] the vaso-

dilatation cannot be explained by beta-2 stimulation. In contrast to what was found before TEA, the net effect of dopamine 4–8 μg · kg^{-1} · min^{-1} during TEA was systemic vasoconstriction. This is consistent with findings in dogs during spinal anesthesia.[26]

CONCLUSION

Provided there is no hypovolemia or prior myocardial failure, low infusion rates of dopamine (approximately 4 μg · kg^{-1} · min^{-1}) are sufficient to achieve cardiovascular stability during an extensive TEA. Volume loading alone did not adequately counteract the hypotensive effect of TEA in this study.

At the higher infusion rate, 8 μg · kg^{-1} · min^{-1}, MAP, CO, and SVR before and during TEA were very similar, in spite of the marked effect of TEA without dopamine. However, this infusion rate carries the risk of inappropriate increases in CVP, PCWP, and MPAP.

References

1. Bonica JJ, Berges PU, Morikawa K: Circulatory effects of peridural block: 1. Effects of level of analgesia and dose of lidocaine. ANESTHESIOLOGY 33:619–626, 1970
2. McLean APH, Mulligan GW, Otton P, MacLean MD: Hemodynamic alterations associated with epidural anesthesia. Surgery 62:79–87, 1967
3. Otton PE, Wilson EJ: The cardiocirculatory effects of upper thoracic epidural analgesia. Can Anaesth Soc J 13:541–549, 1966
4. Reiz S, Nath S, Pontén E: Hemodynamic effects of prenalterol, a beta^1-adrenoceptor agonist in hypotension induced by high thoracic epidural block in man. Acta Anaesthesiol Scand 23: 93–96, 1979
5. Ottesen S, Renck H, Jynge P: I. Thoracic epidural analgesia. Acta Anaesthesiol Scand (Suppl) 69:1–16, 1978
6. Engberg G, Wiklund L: The circulatory effects of intravenously administered ephedrine during epidural blockade. Acta Anaesthesiol Scand (Suppl) 66:27–36, 1978
7. Goldberg LI: Cardiovascular and renal actions of dopamine: Potential clinical applications. Pharmacol Rev 24:1–29, 1972
8. Goldberg LI: Dopamine—Clinical uses of an endogenous catecholamine. N Engl J Med 291:707–710, 1974
9. Järnberg PO, Bengtsson L, Ekstrand J, Hamberger B: Dopamine infusion in man. Plasma catecholamine levels and pharmacokinetics. Acta Anaesthesiol Scand 25:328–331, 1981
10. Clark RB, Brunner JA: Dopamine for the treatment of spinal hypotension during cesarean section. ANESTHESIOLOGY 53:76–79, 1980
11. Yoshida T, Dan K, Tanaka K, Sakimura M: Effects of dopamine and dobutamine on hypotension related to epidural analgesia (in Japanese). Masui 32:680–687, 1983
12. Werner O, Benthin M: Mean intravascular pressure without tears. Simultaneous recording of the unfiltered pressure curve and of mean pressure. Anaesthesia 37:836–837, 1982
13. Eriksson BM, Persson BA: Determination of catecholamines in rat heart tissue and plasma samples by liquid chromatography

with electrochemical detection. J Chromatogr 228:143–154, 1982

14. Sokal RR, Rohlf FJ: Biometry. New York, WH Freeman and Company, 1981, p 385

15. Levinson PD, Goldstein DS, Manson PJ, Gill JR, Keiser H: Endocrine, renal and hemodynamic responses to graded dopamine infusions in normal men. J Clin Endocrinol Metab 60:821–826, 1985

16. Silverberg AB, Shah SD, Haymond MW, Cryer PE: Norepinephrine: hormone and neurotransmitter in man. Am J Physiol 234: 252–256, 1978

17. Horwitz D, Fox SM, Goldberg LI: Effects of dopamine in man. Circ Res 10:237–243, 1962

18. McDonald RH, Goldberg LI, McNay JL, Tuttle EP: Effects of dopamine in man: Augmentation of sodium excretion, glomerular filtration rate and renal plasma flow. J Clin Invest 43: 1116–1124, 1964

19. Mark AL, Iizuka T, Wendling MG, Eckstein JW: Responses of saphenous and mesenteric veins to administration of dopamine. J Clin Invest 49:259–266, 1970

20. Grund E, Müller-Ruchholtz ER, Hauer F, Lapp ER: Effects of dopamine on total peripheral resistance and integrated systemic venous blood volume in dogs. Basic Res Cardiol 75:623–634, 1980

21. Beregovich J, Bianchi C, Rubler S, Lomnitz E, Cagin N, Levitt B: Dose-related hemodynamic and renal effects of dopamine in congestive heart failure. Am Heart J 87:550–557, 1974

22. Harrison DC, Pirages S, Robinson SC, Wintroub BU: The pulmonary and systemic circulatory response to dopamine infusion. Br J Pharmacol 37:618–626, 1969

23. 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

24. Jorfeldt L, Löfström B, Pernow B, Persson B, Wahren J, Widman B: The effect of local anaesthetics on the central circulation and respiration in man and dog. Acta Anaesthesiol Scand 12: 153–169, 1968

25. Ottesen S: The influence of thoracic epidural analgesia on the circulation at rest and during physical exercise in man. Acta Anaesthesiol Scand 22:537–547, 1978

26. Butterworth JF, Johnson MD, Berritzbeitia LD, Austin JC, Dance GR, Cohn LH: Effects of total spinal anesthesia on the response of the peripheral circulation to dopamine and dobutamine (abstract). ANESTHESIOLOGY 63:A213, 1985

27. Lokhandwala MF, Barrett RJ: Cardiovascular dopamine receptors: Physiological, pharmacological and therapeutic implications. J Auton Pharmacol 3:189–215, 1983

28. Lokhandwala MF, Jandhyala BS: The role of sympathetic nervous system in the vascular actions of dopamine. J Pharmacol Exp Ther 210:120–126, 1979

29. Bromage PR: Epidural Analgesia. Philadelphia, WB Saunders, 1978, pp 350–355