

## Systemic and Regional Blood Flow during Epidural Anesthesia without Epinephrine in the Rhesus Monkey

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The radioactive-microsphere technique was used to determine distribution of cardiac output and regional blood flow in rhesus monkeys before and 10, 20, 40, and 80 minutes after induction of epidural anesthesia with lidocaine (1 per cent) without epinephrine. Four monkeys were studied during low epidural anesthesia (sensory level T10) and five other monkeys were studied during high epidural anesthesia (sensory level T1). During T10 epidural anesthesia, blood flow (per 100 g tissue) to the lower extremity was significantly increased 10 minutes after induction of anesthesia. There was no other significant change in regional blood flow during T10 epidural anesthesia. During T1 epidural anesthesia, blood flow to the heart was significantly reduced at 10 minutes, blood flow to the liver was significantly reduced at 10 and 40 minutes, blood flows to kidneys and miscellaneous organs (lymph nodes, salivary glands, etc.) were significantly reduced at 10, 20, and 40 minutes, and blood flow to the brain was significantly reduced throughout anesthesia. Vascular resistance in the lower extremity was reduced in each monkey following epidural anesthesia, indicating arteriolar dilatation. Also, during both levels of anesthesia, the lungs received an increased proportion of the microspheres, suggesting an increased peripheral arteriovenous shunting of microspheres due to the arteriolar dilatation. (Key words: Anesthetic techniques, peridural, hemodynamics; Heart, blood flow; Brain, blood flow; Kidney, blood flow; Liver, blood flow.)

**SIMULTANEOUS MEASUREMENTS of blood flows to various organs during epidural anes-**

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thetia without epinephrine have not been studied either in animal or in man. This has resulted in a lack of knowledge of how cardiac output may be redistributed during anesthesia. The radioactive-microsphere technique enables simultaneous measurement of blood flows to all organs and tissue by injection of non-recirculating microspheres into the left ventricle.<sup>1</sup> The microspheres are distributed to each organ in direct proportion to its blood flow. Injection of microspheres with different isotope labels at various intervals permits repeated measurements of regional blood flow in the same animal.

We utilized this technique to study systemic and regional blood flow changes in rhesus monkeys, during epidural anesthesia without epinephrine, at two dermatome levels of sensory block.

### Materials and Methods

The subjects of the study were nine monkeys (*Macaca mulatta*), weighing 3.9 to 7.3 kg. Three to five days before the experiment, catheters were placed in the inferior vena cava, abdominal aorta, and left ventricle of the heart as described previously.<sup>2</sup> On the day of the experiment, using methohexital (30–60 mg) sedation, 20-gauge Teflon catheters were placed in the epidural space via the sacral hiatus and advanced to about the level of L1–2. After insertion of the epidural catheter, the monkeys were tilted to a supine position in their restraining chairs and placed in sound-protected booths. Room air with a 3–5 l/min flow of oxygen was continuously pumped into the booths to maintain  $P_{a_{O_2}}$  around 70–140 torr. All catheters were brought outside the booths and connected to Statham strain gauges placed at midthoracic levels; thus all measurements of infusions and blood sampling could be per-

formed without disturbing the animal. After sufficient time for recovery from methohexital (1-1½ hours), baseline measurements were carried out. Arterial, central venous and left ventricular pressures were continuously recorded on a Sanborn 150 recorder. Cardiac outputs were determined in duplicate by the indicator dye-dilution technique using indocyanine green. All blood was returned to the animal after the dye-dilution curve had been obtained. Immediately after each cardiac output determination and injection of radioactive microspheres, arterial blood was analyzed for pH, P<sub>O<sub>2</sub></sub> and P<sub>CO<sub>2</sub></sub>.

After baseline measurements had been obtained, lidocaine (1 per cent) without epinephrine was injected through the epidural catheter: 10-30 mg for low epidural anesthesia (sensory level approximately T10) and 40-80 mg for high epidural anesthesia (sensory level approximately T1). Four monkeys were studied during low epidural anesthesia and five monkeys were studied during high epidural anesthesia. Level of anesthesia was confirmed by response of the animal to towel clip application to consecutive dermatomes and correlated with decrease in arterial blood pressure and paralysis of lower extremity; in high-level blocks upper-extremity weakness was the end point. Four subsequent sets of blood flow measurements were made 10, 20, 40, and 80 minutes after lidocaine had been injected. No fluid was administered other than that used in flushing the catheters between measurements.

The distribution of blood flow to various organs was determined at each time interval by injecting a suspension of one of the five gamma-emitting nuclide-labelled microspheres (50 μm in diameter) into the left ventricle after each cardiac output determination. The microspheres are distributed to each organ in proportion to its blood flow and are trapped in the organ arterioles. The following nuclide labels were used: <sup>46</sup>scandium, <sup>93</sup>niobium, <sup>85</sup>strontium, <sup>51</sup>chromium and <sup>141</sup>cerium.

At the end of the experiment the animal was exsanguinated under sodium thiopental anesthesia and the organs and tissues removed, weighed to 0.1 g, and placed in plastic vials. Radioactivity in each vial containing part or all of the organ was measured

in a Packard NaI scintillation counter. All of the tissues from the major organs were counted to determine the radioactivity in these organs. However, only 20 per cent representative samples of skin, muscles, bones, and fat were counted, and these counts were multiplied by 5 to give the total counts for these tissues.

Energy distribution patterns were recorded on a pulse height analyzer set to divide the output of the scintillation counter into 1,024 channels of 1 kev each. Since the five nuclides used in an experiment emitted gamma rays at different but definite energy levels in the 0-1000 kev range, the amount of radioactivity from each isotope in each vial could be determined. The composite emission spectrum from each vial, representing five isotopes, was processed by a PDP-15 digital computer to give individual counts of all five isotopes in each vial. After all organs and tissues had been counted and processed to give the amount of each of the five nuclides present, the total body count of each nuclide was derived by summation of counts of each nuclide from individual organs and tissues. The percentage of cardiac output to each organ was calculated as the amount of radioactivity of each nuclide in that organ divided by total body count of that nuclide. Flow to each organ was the percentage of cardiac output times the cardiac output calculated from the dye-dilution curves obtained immediately prior to injection of that particular nuclide. Right leg blood flow was taken as indicative of lower extremity blood flow since the left leg had been rendered ischemic in the process of placing the arterial catheter.

The baseline regional blood flow to each organ was expressed as the percentage of cardiac output received by that organ and as the absolute blood flow through it (ml/100 g tissue/min). The changes in systemic hemodynamic measurements and the changes in regional blood flow values in each monkey were compared with the baseline values for the same animal, using Student's *t* test for paired observations. Changes during T10 epidural anesthesia were compared with changes during T1 epidural anesthesia using a Student's *t* test for group means. Changes were considered significant when *P* was less than 0.05.

## Results

The systemic hemodynamic values and arterial  $pH$ ,  $P_{O_2}$  and  $P_{CO_2}$  values are shown in tables 1 and 2 and figure 1. During T10 epidural anesthesia the only significant changes were an 18 per cent decrease in mean arterial pressure (MAP) 20 minutes after injection of lidocaine and an 11 per cent decrease in cardiac output ( $Q_t$ ) at 10 minutes. T1 epidural anesthesia decreased MAP (14 to 47 per cent) for the first 40 minutes and decreased  $Q_t$  (30 per cent) for the first 20 minutes. These changes were statistically significant. Total peripheral resistance (TPR) showed no significant change during either level of anesthesia.

Regional blood flow alterations during T10 epidural anesthesia were minimal (table 3 and figures 2 and 3). Blood flows to the major

organs were not altered significantly. The right leg (non-ischemic) received a significantly increased percentage of the  $Q_t$  and absolute blood flow for the first 10 minutes.

Regional blood flow values during T1 epidural anesthesia are shown in table 4 and figures 2 and 3. The percentages of  $Q_t$  received by the heart, brain, and liver did not change significantly, while the absolute blood flows to these organs showed significant decreases; in the brain, this decrease lasted throughout epidural anesthesia. Both the percentages of  $Q_t$  and absolute blood flows to kidneys and organs and tissues grouped under "miscellaneous" (testes, penis, bladder, salivary glands, thyroid, adrenals, major vessels and nerves, trachea, esophagus, tongue, fat, lymph nodes, etc.) were decreased significantly. Blood flows to the lungs and the right

TABLE 1. Systemic Hemodynamic Values during T<sub>10</sub> Epidural Anesthesia in Four Monkeys (Mean  $\pm$  SD)

	Control	10 Minutes	20 Minutes	40 Minutes	80 Minutes
Heart rate (beats/min)	183 $\pm$ 23	197 $\pm$ 22	189 $\pm$ 25	195 $\pm$ 18	191 $\pm$ 32
Mean arterial pressure (torr)	110 $\pm$ 7	81 $\pm$ 12	90 $\pm$ 7*	102 $\pm$ 7	104 $\pm$ 12
Cardiac output (ml/kg/min)	307 $\pm$ 28	272 $\pm$ 34*	275 $\pm$ 44	264 $\pm$ 48	260 $\pm$ 37
Total peripheral resistance (torr/l/min)	71.48 $\pm$ 16.12	62.01 $\pm$ 25.10	69.96 $\pm$ 34.72	80.50 $\pm$ 31.12	81.69 $\pm$ 30.0
$pH$	7.57 $\pm$ 0.02	7.55 $\pm$ 0.04	7.54 $\pm$ 0.02	7.53 $\pm$ 0.04	7.56 $\pm$ 0.02
$P_{O_2}$ (torr)	98 $\pm$ 28	91 $\pm$ 26	112 $\pm$ 24	114 $\pm$ 16	102 $\pm$ 2
$P_{CO_2}$ (torr)	36 $\pm$ 2	38 $\pm$ 4	37 $\pm$ 1	38 $\pm$ 4	37 $\pm$ 4

\*  $P < 0.05$ .

TABLE 2. Systemic Hemodynamic Values during T<sub>1</sub> Epidural Anesthesia in Five Monkeys (Mean  $\pm$  SD)

	Control	10 Minutes	20 Minutes	40 Minutes	80 Minutes
Heart rate (beats/min)	191 $\pm$ 33	170 $\pm$ 20	172 $\pm$ 14	175 $\pm$ 14	181 $\pm$ 20
Mean arterial pressure (torr)	120 $\pm$ 21	63 $\pm$ 7†	79 $\pm$ 14†	103 $\pm$ 19*	117 $\pm$ 20
Cardiac output (ml/kg/min)	306 $\pm$ 77	207 $\pm$ 78†	213 $\pm$ 49*	241 $\pm$ 52	259 $\pm$ 79
Total peripheral resistance (torr/l/min)	64.50 $\pm$ 21.03	53.51 $\pm$ 20.47	61.09 $\pm$ 16.85	71.41 $\pm$ 24.98	77.99 $\pm$ 29.89
$pH$	7.55 $\pm$ 0.02	7.57 $\pm$ 0.01	7.57 $\pm$ 0.02	7.55 $\pm$ 0.02	7.55 $\pm$ 0.02
$P_{O_2}$ (torr)	100 $\pm$ 19	110 $\pm$ 20	111 $\pm$ 21	117 $\pm$ 26	120 $\pm$ 28
$P_{CO_2}$ (torr)	37 $\pm$ 4	36 $\pm$ 5	37 $\pm$ 5	38 $\pm$ 6	38 $\pm$ 4

\*  $P < 0.05$ .

†  $P < 0.01$ .

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leg showed transient but significant increases. Blood flow to the carcass showed no significant change.

Regional vascular resistances per 100 g tissue for major organs and right leg are shown in table 5. Though some of the changes were statistically significant, they were not consistent. For example, during T1 epidural anesthesia the vascular resistance in the brain was decreased significantly at 10 minutes but increased significantly at 80 minutes. Even though the mean vascular resistance in the right leg did not show statistically significant changes due to the large standard deviation, it was decreased in each of the nine monkeys in the entire study (both levels) after induction of epidural anesthesia.

### Discussion

We did not observe any significant variation in rectal temperature, hematocrit, or arterial pH,  $P_{O_2}$  and  $P_{CO_2}$  values during either level of epidural anesthesia. The seemingly alkalotic pH values with near-normal  $P_{CO_2}$  values in awake restrained monkeys have been reported before.<sup>2-4</sup>

### SYSTEMIC HEMODYNAMICS

Previous reports<sup>5,6</sup> have documented that the severity of hypotension is proportional to the height of segmental blockade, and our findings of greater decreases in MAP during T1 epidural anesthesia concur with these findings. However, our findings of significant decreases in  $Q_t$  during both levels of anesthesia are at variance with previous reports.<sup>7-10</sup> Bonica *et al.*,<sup>7</sup> Kennedy *et al.*,<sup>8,9</sup> and Wahba *et al.*<sup>10</sup> reported no change in  $Q_t$  during high epidural anesthesia (T4-5) induced with lidocaine. Bonica<sup>11</sup> concluded that the lack of significant hemodynamic effects was due to 1) compensation achieved by increased baroreceptor reflex activity via the unblocked cardiac sympathetic segments (T1 and T2) resulting in an increased  $Q_t$ , and 2) cardiovascular stimulation due to systemically absorbed lidocaine. Evidence in the literature suggests that small to moderate doses of lidocaine produce cardiovascular stimulation<sup>12,13</sup> and large doses of lidocaine depress the circulation.<sup>14</sup> Bromage and Rob-

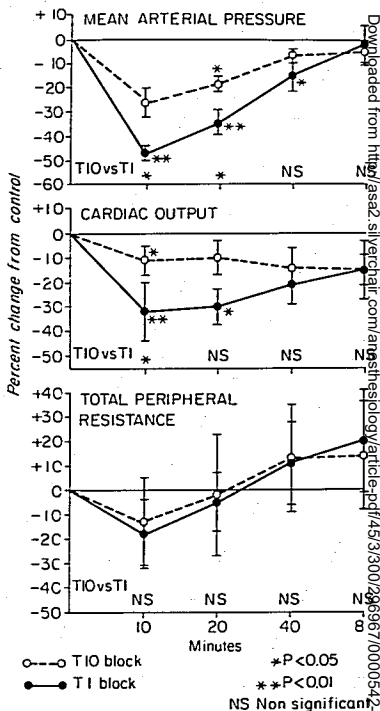


FIG. 1. Effects of T10 and T1 epidural anesthesia without epinephrine on mean arterial pressure, cardiac output, and total peripheral resistance. The values at each time interval are mean percentage changes from control  $\pm$  SE of the mean. Statistical significance compared with control is indicated next to the data points and statistical significance of differences between T10 and T1 epidural anesthesia is indicated on the horizontal axis.

son,<sup>15</sup> from their study of human volunteers, concluded that for epidural anesthesia the dose of lidocaine without epinephrine should not exceed 7-8 mg/kg body weight. In our study, the dose of lidocaine for T10 epidural anesthesia did not exceed 5 mg/kg, and for T1 epidural anesthesia the dose was less than 8 mg/kg in all monkeys except one, which

TABLE 3. Regional Blood Flow during T<sub>100</sub> Epidural Anesthesia in Four Monkeys (Mean ± SD)

	Control	10 Minutes	20 Minutes	40 Minutes	80 Minutes
Heart Per cent $\dot{Q}_t$ Flow/100 g/min	4.73 ± 0.84 357 ± 68	4.00 ± 1.61 269 ± 118	4.80 ± 1.12 318 ± 41	5.85 ± 1.54 375 ± 95	4.78 ± 1.57 290 ± 80
Brain Per cent $\dot{Q}_t$ Flow/100 g/min	4.40 ± 0.96 60 ± 7	5.13 ± 2.48 68 ± 18	5.05 ± 2.18 68 ± 8	4.65 ± 2.31 59 ± 10	4.20 ± 1.88 57 ± 14
Kidneys Per cent $\dot{Q}_t$ Flow/100 g/min	12.08 ± 4.25 701 ± 243	13.73 ± 2.73 716 ± 188	12.33 ± 1.57 650 ± 143	10.63 ± 1.12 537 ± 124	11.23 ± 2.37 568 ± 124
Liver (hepatic artery and portal vein) Per cent $\dot{Q}_t$ Flow/100 g/min	18.83 ± 6.68 212 ± 87	18.00 ± 2.22 179 ± 44	21.45 ± 4.18 220 ± 75	18.58 ± 4.82 185 ± 85	18.05 ± 6.30 176 ± 83
Lungs Per cent $\dot{Q}_t$ Flow/100 g/min	0.25 ± 0.11 13 ± 6	1.74 ± 1.07 68 ± 37	1.41 ± 1.31 53 ± 39	0.97 ± 1.30 30 ± 32	0.76 ± 0.84 27 ± 24
Right leg (non-ischemic) Per cent $\dot{Q}_t$ Flow/100 g/min	5.30 ± 2.06 13 ± 6	8.10 ± 2.06* 17 ± 6*	6.35 ± 1.16 14 ± 5	6.03 ± 1.65 12 ± 5	6.40 ± 1.88 13 ± 5
Carcass§ Per cent $\dot{Q}_t$ Flow/100 g/min	43.78 ± 7.65 28 ± 6	35.33 ± 4.19 20 ± 2	38.00 ± 6.33 22 ± 4	43.43 ± 4.50 24 ± 3	39.13 ± 4.97 22 ± 3
Miscellaneous§ Per cent $\dot{Q}_t$ Flow/100 g/min	5.83 ± 2.46 46 ± 22	4.43 ± 0.52 31 ± 5	5.08 ± 1.62 35 ± 8	5.08 ± 2.90 33 ± 17	7.88 ± 4.97 53 ± 37

\*  $P < 0.05$ .

† Portal vein flow is the sum of blood flows to GI tract, mesentery, pancreas and spleen.

‡ Carcass includes spinal cord and all skin, muscles and bones other than those of the right and left legs.

§ Miscellaneous includes testes, penis, bladder, salivary glands, thyroid, adrenals, major vessels and nerves, trachea, esophagus, tongue,

TABLE 4. Regional Blood Flow during T<sub>1</sub> Epidural Anesthesia in Five Monkeys (Mean ± SD)

	Control	10 Minutes	20 Minutes	40 Minutes	80 Minutes
<b>Heart</b>					
Per cent $\dot{Q}_t$	6.62 ± 1.74	4.57 ± 0.72	5.48 ± 1.12	5.87 ± 1.38	6.71 ± 1.27
Flow/100 g/min	512 ± 184	246 ± 117*	299 ± 87	354 ± 84	445 ± 164
<b>Brain</b>					
Per cent $\dot{Q}_t$	4.13 ± 0.53	4.39 ± 1.70	4.67 ± 1.56	3.68 ± 0.87	3.90 ± 1.19
Flow/100 g/min	82 ± 11	55 ± 9†	63 ± 14†	62 ± 9*	65 ± 8*
<b>Kidneys</b>					
Per cent $\dot{Q}_t$	14.48 ± 3.33	14.57 ± 4.19	14.65 ± 3.49	11.74 ± 1.78*	12.10 ± 3.40†
Flow/100 g/min	979 ± 350	652 ± 292†	680 ± 193*	617 ± 136*	686 ± 300
<b>Liver (hepatic artery and portal vein†)</b>					
Per cent $\dot{Q}_t$	20.98 ± 2.83	19.34 ± 3.48	22.08 ± 3.70	18.78 ± 3.17	22.10 ± 9.66
Flow/100 g/min	264 ± 53	159 ± 37†	194 ± 56	190 ± 55*	256 ± 120
<b>Lungs</b>					
Per cent $\dot{Q}_t$	0.54 ± 0.35	2.24 ± 0.81†	3.12 ± 2.61	1.39 ± 1.20	0.38 ± 0.22
Flow/100 g/min	33 ± 24	91 ± 56*	142 ± 136	69 ± 63	20 ± 15
<b>Right leg (non-ischemic)</b>					
Per cent $\dot{Q}_t$	5.23 ± 1.11	8.07 ± 2.26*	8.02 ± 2.86	5.54 ± 1.55	4.62 ± 1.82
Flow/100 g/min	13 ± 5	13 ± 5	14 ± 6	11 ± 5	9 ± 4
<b>Carcass‡</b>					
Per cent $\dot{Q}_t$	34.76 ± 3.57	32.60 ± 7.64	32.04 ± 7.48	42.58 ± 8.82	38.14 ± 11.85
Flow/100 g/min	23 ± 9	14 ± 5	15 ± 4	23 ± 4	22 ± 11
<b>Miscellaneous§</b>					
Per cent $\dot{Q}_t$	9.50 ± 2.87	5.98 ± 1.85†	6.08 ± 1.54*	5.32 ± 1.11*	8.60 ± 2.55
Flow/100 g/min	50 ± 16	21 ± 8†	24 ± 12†	25 ± 13†	42 ± 24

\*  $P < 0.05$ .

†  $P < 0.01$ .

‡ Portal vein flow is the sum of blood flows to the GI tract, mesentery, pancreas and spleen.

§ Carcass includes spinal cord and all skin, muscles and bones other than those of the right and left legs.

¶ Miscellaneous includes testes, penis, bladder, salivary glands, thyroid, adrenals, major vessels and nerves, trachea, esophagus, tongue,

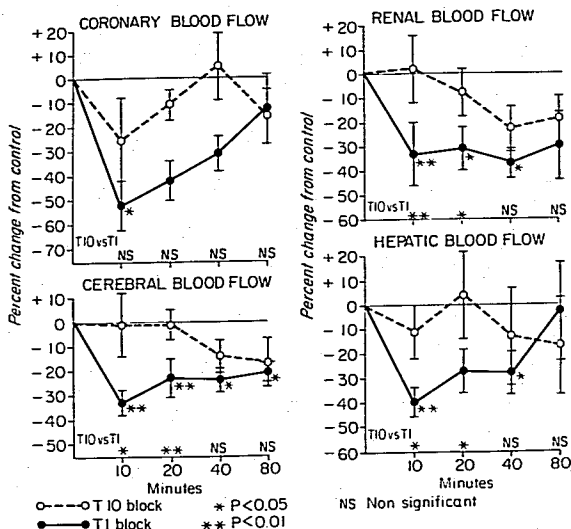


FIG. 2. Effects of T10 and T1 epidural anesthesia without epinephrine on coronary, cerebral, renal, and hepatic blood flows. The values at each time interval are mean percentage changes from control  $\pm$  SE of the mean. Blood flow is expressed as flow in ml/100 g of tissue/min. Statistical significance compared with control is indicated next to the data points and statistical significance of differences between T10 and T1 epidural anesthesia is indicated on the horizontal axis.

received 12 mg/kg inadvertently. In two other monkeys not included in the study, we measured serum lidocaine levels after injecting 12 mg/kg lidocaine epidurally. Peak serum lidocaine level was 5.78  $\mu$ g/ml in one animal and 8.04  $\mu$ g/ml in the other. Munson *et al.*<sup>16</sup> observed consistent elevations of systolic blood pressure and pulse rate and no sign of cardiovascular depression in rhesus monkeys after intravenous infusions of lidocaine that resulted in a mean serum lidocaine level of 24.5  $\mu$ g/ml. Hence it is unlikely that the cardiovascular depression that we observed during both levels of anesthesia was due to systemic effects of lidocaine. It is probable that our monkeys, though acclimatized to the restraining chairs for three to five days, were excited and had high sympathetic tone. Subjects who have high sympathetic tone provoked by apprehension,

injury, or disease have much greater hemodynamic changes when the sympathetic tone is removed.<sup>17</sup> In addition, during T1 epidural anesthesia in our monkeys, blockade of cardiac sympathetic fibers arising from the upper four or five thoracic nerves may have contributed to the cardiovascular depression.<sup>18</sup>

We observed no significant change in total peripheral resistance during either level of epidural anesthesia. We had postulated that this might be due to increased renin-angiotensin activity in response to decreased MAP.<sup>2</sup> Recent measurements of renin-angiotensin activity in dogs during total sympathetic blockade induced by spinal anesthesia support this hypothesis.<sup>§</sup>

§ Amory DW (Department of Anesthesiology, University of Washington, Seattle, Washington 98195): Personal communication.

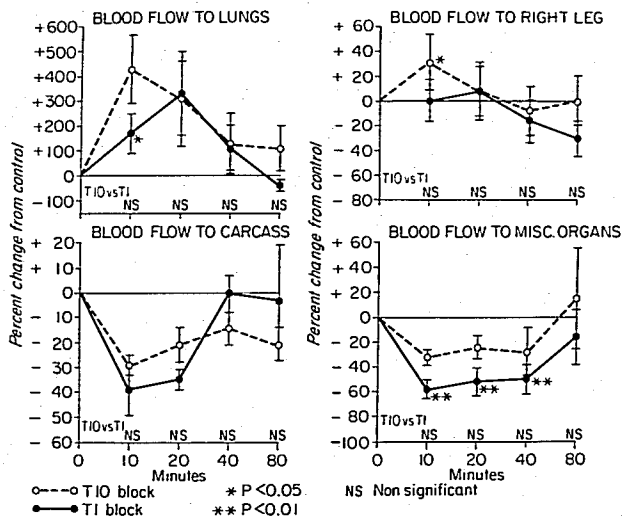


FIG. 3. Effects of T10 and T1 epidural anesthesia without epinephrine on blood flows to the lungs, right leg, carcass and miscellaneous organs. The values at each time interval are mean percentage changes from control  $\pm$  SE of the mean. Blood flow is expressed as flow in ml/100 g of tissue/min. Statistical significance compared with control is indicated next to the data points and statistical significance of differences between T10 and T1 epidural anesthesia is indicated on the horizontal axis.

TABLE 5. Regional Vascular Resistance during T<sub>10</sub> (n = 4) and T<sub>1</sub> (n = 5) Epidural Anesthesia (Mean  $\pm$  SD)

	Control	10 Minutes	20 Minutes	40 Minutes	80 Minutes
Heart					
T10	0.32 $\pm$ 0.08	0.33 $\pm$ 0.10	0.28 $\pm$ 0.03	0.28 $\pm$ 0.07	0.36 $\pm$ 0.12
T1	0.26 $\pm$ 0.10	0.30 $\pm$ 0.13	0.28 $\pm$ 0.07	0.31 $\pm$ 0.11	0.30 $\pm$ 0.16
Brain					
T10	1.60 $\pm$ 0.21	1.21 $\pm$ 0.16	1.34 $\pm$ 0.15†	1.77 $\pm$ 0.30	1.89 $\pm$ 0.38
T1	1.46 $\pm$ 0.25	1.16 $\pm$ 0.15*	1.30 $\pm$ 0.33	1.70 $\pm$ 0.44	1.84 $\pm$ 0.50*
Kidneys					
T10	0.17 $\pm$ 0.05	0.11 $\pm$ 0.03*	0.14 $\pm$ 0.04	0.19 $\pm$ 0.04	0.18 $\pm$ 0.03
T1	0.13 $\pm$ 0.05	0.11 $\pm$ 0.04	0.12 $\pm$ 0.03	0.17 $\pm$ 0.06*	0.19 $\pm$ 0.09
Liver					
T10	0.60 $\pm$ 0.29	0.47 $\pm$ 0.16	0.47 $\pm$ 0.24*	0.64 $\pm$ 0.29	0.69 $\pm$ 0.32*
T1	0.48 $\pm$ 0.20	0.41 $\pm$ 0.11	0.42 $\pm$ 0.11	0.59 $\pm$ 0.24	0.55 $\pm$ 0.29
Right leg					
T10	10.34 $\pm$ 4.82	5.07 $\pm$ 1.23	7.45 $\pm$ 3.36	9.91 $\pm$ 5.67	9.24 $\pm$ 4.37
T1	10.65 $\pm$ 6.08	5.61 $\pm$ 2.64	6.51 $\pm$ 2.99	11.57 $\pm$ 6.22	15.57 $\pm$ 8.05

Regional vascular resistance is expressed as torr/ml/100 g of tissue/min.

\* P < 0.05.

† P < 0.01.



TABLE 6. Coronary Blood Flow vs. Cardiac Work during T<sub>1</sub> Epidural Anesthesia

	10 Minutes	20 Minutes	40 Minutes	80 Minutes
Mean change in flow/100 g (per cent)	-52	-42	-31	-14
Mean change in cardiac work/min (per cent)	-64	-53	-32	-18

## REGIONAL BLOOD FLOW

Lidocaine without epinephrine when injected into the epidural space rapidly enters the systemic circulation within a few minutes.<sup>19</sup> Therefore, in discussing the effects of epidural anesthesia on organ blood flow, the effects of systemically absorbed lidocaine have to be taken into account. Bloor and White<sup>20</sup> observed in unanesthetized dogs that a small bolus of lidocaine (0.25 mg/kg, iv) produces an increase in coronary blood flow, whereas large doses (2 mg/kg, iv) decrease coronary blood flow. Thomsen *et al.*<sup>21</sup> reported a 14 per cent decrease in coronary blood flow in anesthetized dogs only after large doses of lidocaine (5 mg/kg bolus followed by steady infusion at the rate of 0.15 mg/kg/min). Serum levels of lidocaine were not reported in either study. It is unlikely, however, that the monkeys in our study achieved similar concentrations of lidocaine in the circulation. Benovitz *et al.*,<sup>22</sup> using the radioactive-microsphere technique, studied the changes in the distribution of  $\dot{Q}_t$  in rhesus monkeys during intravenous infusions of lidocaine. At serum lidocaine levels ranging from 1.2 to 2.4  $\mu\text{g/ml}$ , they observed significant increases in the percentages of  $\dot{Q}_t$  received by the heart, hepatic artery and long bones, while MAP and total  $\dot{Q}_t$  remained unchanged. We did not observe such increases during either level of epidural anesthesia. It is likely that with the significant reductions in MAP and  $\dot{Q}_t$  that we observed during both levels of anesthesia, any increase in blood flows to the heart, hepatic artery, and long bones caused by systemic lidocaine could have been abolished. Sakabe *et al.*<sup>23</sup> found that subseizure doses of lidocaine had no effect on cerebral blood flow in dogs, and that doses capable of inducing seizures markedly increased cerebral blood flow. Therefore, we conclude that the decreases in cerebral blood flow that we observed during T<sub>1</sub> epidural anesthesia were

not due to lidocaine in the systemic circulation.

T<sub>10</sub> EPIDURAL ANESTHESIA

It appears that the moderate decreases in MAP (18 per cent) and  $\dot{Q}_t$  (11 per cent) are insufficient to cause significant changes in regional blood flow. These findings are similar to those we observed earlier during low spinal anesthesia in rhesus monkeys.<sup>2</sup>

T<sub>1</sub> EPIDURAL ANESTHESIA

In our study, the transient but significant decrease in coronary blood flow (52 per cent at 10 minutes) paralleled the reduction in MAP (47 per cent). This agrees with the findings of Eckenhoff *et al.*<sup>24</sup> and Hackett *et al.*,<sup>25</sup> who studied coronary blood flow changes during hypotension induced by intravenous administration of tetraethyl ammonium chloride or spinal anesthesia. Even though coronary blood flow decreased significantly, myocardial minute work calculated as the product of MAP and  $\dot{Q}_t$  decreased more than the decrease in coronary blood flow (table 6). This indicates adequate perfusion relative to myocardial work load.

Cerebral blood flow is maintained over a range of perfusion pressures from 60 to 150 torr.<sup>26</sup> This autoregulation maintains cerebral blood flow during hypotension resulting from spinal anesthesia.<sup>27</sup> However, we did not observe autoregulation in our monkeys. With the decreases in MAP, cerebral blood flow decreased throughout the duration of anesthesia. Cerebrovascular resistance showed inconsistent changes. Galindo<sup>28</sup> reported significant decreases in internal carotid blood flow in dogs following epidural anesthesia with lidocaine. Kusumoto<sup>29</sup> used mepivacaine to induce epidural anesthesia in human subjects and observed increases in lactate:pyruvate ratio and excess lactate in the internal jugular venous blood, suggesting rela-

tive hypoxia and decreased cerebral blood flow. While lidocaine has no effect on cerebral blood flow,<sup>23</sup> the above-mentioned studies<sup>24,29</sup> and ours suggest a possible effect of lidocaine and mepivacaine on cerebral autoregulation. Further work in this area is indicated.

Autoregulation also plays a role in the maintenance of blood flow to kidneys over a range of perfusion pressures from 80 to 180 torr.<sup>30</sup> But in human subjects, Kennedy *et al.*<sup>9</sup> found a significant 14 per cent reduction in renal blood flow during high (T5) epidural anesthesia without epinephrine, without concomitant change in MAP and  $\dot{Q}_i$ . The greater decreases in renal blood flow (31 to 37 per cent) that we observed were accompanied by significant decreases in MAP and  $\dot{Q}_i$ . These findings suggest that renal autoregulation might also be affected during high epidural anesthesia induced with lidocaine.

Total hepatic blood flow (sum of hepatic-artery and portal-vein flows) is dependent on MAP.<sup>31</sup> With 14 to 47 per cent decreases in MAP, we observed 28 to 40 per cent decreases in total hepatic blood flow. This agrees with the findings of Kennedy *et al.*<sup>9</sup> in human volunteers. Portal-vein flow in our studies was computed as the sum of arterial flows to the GI tract, mesentery, pancreas and spleen, since the microsphere technique measures only arterial flows directly. The microspheres do not enter the portal circulation as a result of entrapment in the arterioles and capillary bed. Changes in arterial flows to GI tract, mesentery, pancreas and spleen paralleled changes in MAP.

The lungs in each of the nine monkeys in the study (both levels of anesthesia) received an increased proportion of the microspheres during anesthesia. This was accompanied by decreases in regional vascular resistance in the lower extremity in each monkey, which indicates arteriolar dilatation. The increase in the lungs probably reflects the microspheres that return to the lungs after passing through peripheral anatomic arteriovenous shunts that open up due to arteriolar dilatation produced by the sympathetic blockade. Evidence for arteriovenous shunting of microspheres has been reported.<sup>1,2,32</sup>

TABLE 7. Comparison of Peak Effects of T1 Spinal Anesthesia and T1 Epidural Anesthesia without Epinephrine (Mean Per Cent Change from Control)

	T1 Spinal	T1 Epidural
Mean arterial pressure	-23*	-47*
Cardiac output	-22*	-32*
Coronary blood flow	-19	-52*
Cerebral blood flow	-18	-33*
Renal blood flow	-36*	-37*
Hepatic blood flow	-23*	-40*

\* Statistically significant change compared with the control for the same group.

Comparing these observations with our earlier findings of systemic and regional blood flow changes during spinal anesthesia in rhesus monkeys,<sup>2</sup> we see greater decreases in MAP and  $\dot{Q}_i$  during epidural anesthesia (table 7). The maximum decreases in MAP were 22 per cent during T1 spinal anesthesia and 47 per cent during T1 epidural anesthesia. Maximum reductions in  $\dot{Q}_i$  were 20 per cent during T1 spinal anesthesia and 32 per cent during T1 epidural anesthesia. Also, coronary and cerebral blood flows were significantly decreased during epidural anesthesia, whereas they showed only non-significant changes during spinal anesthesia. The greater reduction in MAP during epidural anesthesia is similar to the observations made by Defalque,<sup>6</sup> but the greater decreases in  $\dot{Q}_i$  during epidural anesthesia differ from findings in a previous study.<sup>7</sup> Although the greater changes during epidural anesthesia could be attributed to lidocaine absorbed from the epidural space, available evidence in the literature does not wholly support this hypothesis.<sup>11-13,15,16,20,23</sup>

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