

sample to various degrees, depending on the physical properties of the different molecules. The resultant ions then are projected into the analyzer compartment where a magnetic field influences the distance the various ions traverse.<sup>1</sup> The charge and mass of the ions determine how the accelerating mechanism and magnetic field distribute the ions on the analyzer's collector plates. The electronic collection plate signals then are translated into digital signals, which are displayed on the screen.

Each of the compounds we monitor, *i.e.*, oxygen, carbon dioxide, nitrogen, nitrous oxide, halothane, enflurane, and isoflurane, have partially unique mass spectral qualities. Because they ionize differently, even isomers such as enflurane and isoflurane can be distinguished by the instrument. The mass spectrometer algorithm is written to calculate the concentrations of the gases as a fraction of their differences and corrects for their mass spectral similarities by a process referred to as spectrum overlap erasing.<sup>2</sup>

The fluorinated hydrocarbon propellants we used

apparently all generate a signal at mass 91, at which a strong isoflurane mass peak also occurs. Without a specific algorithm to erase the spectrum overlap for the propellant, the unit interpreted it as isoflurane. This problem did not occur in tests we conducted with the Chemetron SARA mass spectrometer system. In the Perkin-Elmer system, the presence of propellant at one sampling station did not affect subsequent measurements from that station or from other stations.

The misleading isoflurane partial pressure secondary to the presence of this type of propellant is avoided easily by not dispensing medication with such a propellant while the spectrometer is sampling.

#### REFERENCES

1. Sodal IE, Swanson GD: Mass spectrometer in patient monitoring, *Essential Noninvasive Monitoring in Anesthesia*. Edited by Gravenstein JS, Newbower RS, Ream AK, Smith NT, Bardeen J. New York, Grune and Stratton, 1980, pp 217-223
2. Gillbe CE, Heneghan CPH, Branthwaite MA: Respiratory mass spectrometry during general anaesthesia. *Br J Anaesth* 53:103-108, 1981

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### Inhibition of Epinephrine Absorption by Dextran

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To obtain optimal local hemostasis in patients undergoing surgery, cutaneous infiltration of a dilute solution of epinephrine is performed. The safe dose of epinephrine for adults under halothane anesthesia has been reported by Katz *et al.*,<sup>1</sup> Johnstone *et al.*,<sup>2</sup> Melgrave,<sup>3</sup> and Wallbank.<sup>4</sup> Recently, Karl *et al.*<sup>5</sup> have demonstrated that children can tolerate greater amounts of epinephrine on a body weight basis than adults. The use of epinephrine together with halothane, however, is still controversial, even when the dose is kept within

the "safe dose." This is because even amounts far smaller than the "safe dose" of epinephrine can produce unfavorable circulatory effects, especially when injected into vascular-rich tissue such as the scalp.<sup>5</sup>

One of the suggested causes of the reaction is a rapid increase in the plasma level of epinephrine.<sup>4</sup> We, therefore, measured the plasma concentration of epinephrine after its injection into the scalp, with the objective of elucidating the causative mechanism of the adverse reaction. This study also was designed to address the effect of dextran, infiltrated concomitantly with epinephrine, on the transfer of epinephrine to the blood.

#### MATERIALS AND METHODS

After obtaining approval from the committee for the protection of human subjects and informed consent, we studied 35 ASA I and II patients who were scheduled for elective craniotomy. The age range was from 35 to 77 yr, and their mean weight was 55 Kg. The anesthesiologists were allowed to choose the agents and

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TABLE 1. Hemodynamic Changes Produced by the Injection (Mean  $\pm$  SD)

Group		Before Injection	Peak Values Produced by the Injection	Per Cent Changes
D (n = 7)	H R	76 $\pm$ 6	86 $\pm$ 11	+12 $\pm$ 11
	S A P	109 $\pm$ 17	125 $\pm$ 22	+15 $\pm$ 11*
	R P P	8.3 $\pm$ 1.2	10.6 $\pm$ 1.8†	+29 $\pm$ 20
LE (n = 14)	H R	76 $\pm$ 15	89 $\pm$ 15‡	+18 $\pm$ 12*
	S A P	105 $\pm$ 16	123 $\pm$ 22‡	+18 $\pm$ 16§
	R P P	8.0 $\pm$ 1.2	11.1 $\pm$ 3.2¶	+39 $\pm$ 22**
LED (n = 14)	H R	74 $\pm$ 14	81 $\pm$ 13	+11 $\pm$ 7
	S A P	107 $\pm$ 12	113 $\pm$ 14	+6 $\pm$ 10
	R P P	7.9 $\pm$ 1.7	9.3 $\pm$ 1.9‡	+19 $\pm$ 16

HR, SAP, and RPP represent heart rate (beats/min), systolic arterial pressure (mmHg), and rate pressure product ( $\times 10^3$ ), respectively.

\*  $P < 0.05$  as compared with Group LED.

†  $P < 0.025$  as compared with the prior value.

‡  $P < 0.05$  as compared with the prior value.

§  $P < 0.025$  as compared with Group LED.

¶  $P < 0.01$  as compared with the prior value.

\*\*  $P < 0.01$  as compared with Group LED.

methods for induction of anesthesia. After the trachea was intubated, the patients were ventilated mechanically to keep the  $\text{Pa}_{\text{CO}_2}$  at 30–35 mmHg. During the 30 min usually required for positioning and preoperative preparation, and the period of the study, anesthesia was maintained with 1 to 2% halothane mixed with 50% nitrous oxide in oxygen or 2 to 2.5% halothane in 100% oxygen. The ECG and the arterial pressure waves from an indwelling catheter were displayed continuously on an oscilloscope, and they also were recorded simultaneously during the study.

The patients were divided randomly into three groups, and three different solutions were prepared for cutaneous injection: 1) 10% low-molecular-weight dextran in saline solution (D,  $n = 7$ ); 2) 1:200,000 epinephrine with 0.5% lidocaine in saline solution (LE,  $n = 14$ ); and 3) 1:200,000 epinephrine with 0.5% lidocaine and 10% low-molecular-weight dextran in saline solution (LED,  $n = 14$ ). After positioning the patient for surgery, one of the three solutions was injected at 0.5 ml/kg into the scalp by an anesthesiologist over a period of 5 min. Half of the solution first was deposited beneath the aponeurosis, followed by infiltration of the remaining half into the subcutaneous tissue.

Arterial blood for analysis of catecholamines was sampled six times, *i.e.*, before injection and 1, 5, 10, 20, and 30 min after completion of the injection. The sampled blood was treated with ethylene-diamine-tetraacetic acid (EDTA) and centrifuged immediately. The plasma was stored in a freezer at  $-25^\circ \text{C}$  and analyzed within three days. The catecholamines were measured by fluorimetric analysis based on the trihydroxyindole reaction. High-performance liquid chromatography was used to determine epinephrine and norepinephrine differentially. The limit of sensitivity of this method was 0.01 ng/ml for each catecholamine.

Results are expressed as the mean  $\pm$  SD. Comparison of variables within groups was made using analysis of variance (ANOVA) and between groups using an un-

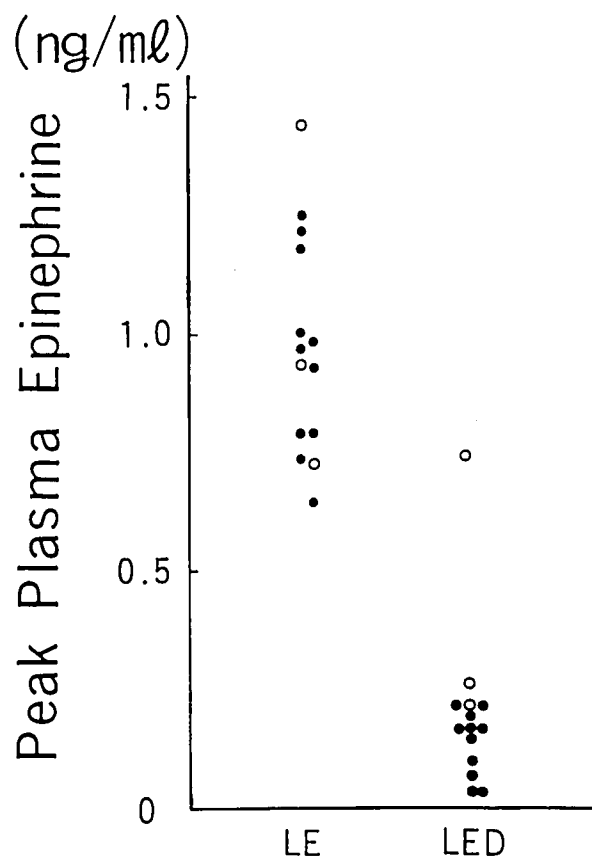


FIG. 1. Peak plasma epinephrine levels following epinephrine injection. Each circle represents one patient. The concentration of plasma epinephrine peaked at 5 min after completion of the injection in 22 out of 28 cases. The empty circles represent the 6 cases in which the plasma epinephrine level peaked at 1 min after completion of the injection.

TABLE 2. The Time Course of Plasma Epinephrine Level (ng/ml) after Injection of the Solution (Mean  $\pm$  SD)

Group	Control	Time after completion of injection				
		1	5	10 (start of surgery)	20	30 (min)
D (n = 7)	<0.01	$\leq 0.02$	$\leq 0.01$	$\leq 0.01$	$0.02 \pm 0.02$	$0.02 \pm 0.02$
LE (n = 14)	<0.01	$0.65 \pm 0.31$	$0.92 \pm 0.26$	$0.53 \pm 0.19$	$0.27 \pm 0.12$	$0.17 \pm 0.08$
LED (n = 14)	<0.01	$0.17 \pm 0.17$	$0.15 \pm 0.08$	$0.10 \pm 0.06$	$0.09 \pm 0.04$	$0.08 \pm 0.05$

The difference in the plasma epinephrine levels among three groups are significant ( $P < 0.005$ ), except in the control values.

paired Student's *t* test. *P* values of less than 0.05 were considered significant.

### RESULTS

Hemodynamic changes produced by the injection are shown in table 1. The peak values were those observed during the period of injection and the 5 min after completion of the injection. Percent changes in heart rate, systolic arterial pressure, and rate pressure product in Group LE were significantly greater than those in Group LED.

The peak plasma epinephrine levels of Groups LE and LED are shown in figure 1. The concentration of plasma epinephrine peaked at 5 min after completion of the epinephrine injection in 22 of 28 cases. In the six remaining cases, the plasma epinephrine levels peaked at one minute after completion of the injection. The time course of the plasma epinephrine levels is shown in table 2. The concentration of plasma epinephrine declined gradually after 5 min in Groups LE and LED but increased after starting surgery in Group D. The differences in the plasma epinephrine levels among the three groups were significant ( $P < 0.005$ ) during the study, but the control values showed no significant deviations.

The plasma level of norepinephrine was unchanged in Groups LE and LED throughout the study but increased by  $167 \pm 10\%$  in Group D by the start of surgery (table 3). Accordingly, the commencement of surgery produced an increase in heart rate and arterial blood pressure in Group D. No such changes occurred in Groups LE and LED (table 4). None of the patients developed serious circulatory complications such as

cardiac arrhythmias or hypertensive episodes due to the use of epinephrine in this study. The hemostatic effect of the injected epinephrine solution was satisfactory in Groups LE and LED.

### DISCUSSION

The results of this study demonstrate that a rapid increase in the plasma level of epinephrine can occur in some cases (fig. 1). This can be one of the causative mechanisms of unfavorable circulatory effects in the use of epinephrine, even when the dose is kept within the "safe dose."

The absorption of epinephrine into the blood is suppressed significantly by the use of 10% low-molecular-weight dextran instead of normal saline solution to dilute the epinephrine (table 2). There has been controversy concerning the action of dextran in prolonging the duration of action of local anesthetics<sup>6-8</sup> (since 1968, when Loder<sup>9</sup> reported on this matter). Scurlock and Curtis<sup>10</sup> demonstrated that dextran has no suppressive action on the absorption of local anesthetic. This study demonstrates the potential of dextran for suppression of the absorption of epinephrine.

A certain degree of hemostatic effect is expected from the injection of dextran alone or, even, saline solution. Attention, however, should be aid to the circulatory reactions produced by the start of surgery. The local anesthetic action of lidocaine was not interfered with by mixing with dextran (tables 3 and 4). The use of a dextran solution containing a local anesthetic and epinephrine is appropriate from the viewpoints of both surgery and anesthesia.

In conclusion, a rapid increase in the plasma level of

TABLE 3. The Time Course of Plasma Norepinephrine Level (ng/ml, Mean  $\pm$  SD)

Group	Control	Time after Completion of the Injection				
		1	5	10 (start of surgery)	20	30 (min)
D (n = 7)	$0.19 \pm 0.08$	$0.20 \pm 0.09$	$0.18 \pm 0.10$	$0.20 \pm 0.13$	$0.40 \pm 0.18^*$	$0.39 \pm 0.20$
LE (n = 11)	$0.16 \pm 0.09$	$0.16 \pm 0.07$	$0.13 \pm 0.05$	$0.12 \pm 0.06$	$0.14 \pm 0.09$	$0.16 \pm 0.09$
LED (n = 11)	$0.13 \pm 0.08$	$0.13 \pm 0.08$	$0.10 \pm 0.05$	$0.10 \pm 0.06$	$0.08 \pm 0.06$	$0.08 \pm 0.07$

\*  $167 \pm 10\%$  increase ( $P < 0.05$ ) as compared with the value prior to surgery within group.

TABLE 4. Hemodynamic Changes Produced by the Surgery (Mean  $\pm$  SD)

Group		Before Surgery	Five Minutes after the Start of Surgery	Per Cent Changes
D (n = 7)	H R	74 $\pm$ 6	89 $\pm$ 11*	+21 $\pm$ 19
	S A P	96 $\pm$ 17	136 $\pm$ 31*	+48 $\pm$ 18
	R P P	7.1 $\pm$ 1.3	12.5 $\pm$ 3.5†	+80 $\pm$ 51
LE (n = 14)	H R	85 $\pm$ 16	85 $\pm$ 16	+1 $\pm$ 2
	S A P	101 $\pm$ 18	100 $\pm$ 16	-1 $\pm$ 7
	R P P	8.7 $\pm$ 2.7	8.6 $\pm$ 2.7	0 $\pm$ 9
LED (n = 14)	H R	80 $\pm$ 12	80 $\pm$ 12	+1 $\pm$ 2
	S A P	97 $\pm$ 14	96 $\pm$ 12	-1 $\pm$ 4
	R P P	7.7 $\pm$ 1.5	7.7 $\pm$ 1.4	0 $\pm$ 5

HR, SAP, and RPP represent heart rate (beat/min), systolic arterial pressure (mmHg), and rate pressure product ( $\times 10^3$ ), respectively.

\*  $P < 0.025$ , † $P < 0.005$  as compared with the prior value.

epinephrine occurs in some cases when an epinephrine solution is injected for hemostatic purposes. The absorption of epinephrine into the blood is suppressed significantly by using 10% low-molecular-weight dextran instead of normal saline solution to dilute the epinephrine.

REFERENCES

1. Katz RL, Matteo RS, Papper EM: The injection of epinephrine during general anesthesia. 2 Halothane. ANESTHESIOLOGY 23:597-600, 1962
2. Jonstone PR, Eger EI II, Wilson C: A comparative interaction of epinephrine with enflurane, isoflurane, and halothane in man. Anesth Analg 55:709-712, 1970
3. Melgrave AP: The use of epinephrine in the presence of halothane in children. Can Anaesth Soc J 17:256-260, 1970

4. Wallbank WA: Cardiac effects of halothane and adrenaline in harelip and cleft palate surgery. Br J Anaesth 42:548-552, 1983
5. Karl HW, Swedlow DB, Lee KW, Downess JJ: Epinephrine halothane interaction in children. ANESTHESIOLOGY 58:142-145, 1983
6. Loder RE: A long acting local anesthetic solution for the relief of pain after thoractomy. Thorax 17:375-376, 1962
7. Chinn MA, Wirjoatmadja K: Prolonging local anesthesia. Lancet 2:835, 1967
8. Kaplan JA, Miller ED, Gallagher EG Jr: Postoperative analgesia for thoracotomy patients. Anesth Analg 54:773-777, 1975
9. Loder RE: A local-anesthetic solution with longer action. Lancet 2:346-347, 1960
10. Scurlock JE, Curtis BM: Dextran-local anesthetic interactions. Anesth Analg 59:335-340, 1980

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Neuromuscular Effects of Atracurium in Infants and Children

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Atracurium is a new short-intermediate acting neuromuscular blocking drug that, with the usual clinical doses in pediatric patients, does not cause any appreciable change in heart rate or blood pressure.<sup>1,2</sup> Its relatively short duration of action makes it a suitable agent for short surgical procedures that are frequent in infants and children.

Previously we studied atracurium in adolescents and children anesthetized with halothane N<sub>2</sub>O:O<sub>2</sub>.<sup>1</sup> In the present study we evaluated the effects of atracurium in infants anesthetized with N<sub>2</sub>O:O<sub>2</sub>:halothane and in children anesthetized with N<sub>2</sub>O:O<sub>2</sub> narcotic technique. We used the same methods of evaluation and measurement as in our previous study to facilitate the comparison between the responses of adolescents, children, and infants.

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