

TABLE 2

Tube	1	2	3	4	5
Procaine (50 mg./ml.) Cerebrospinal fluid Blood	5 mg. 0.9 ml. 10 μ l.	5 mg. 0.9 ml. 20 μ l.	5 mg. 0.9 ml. 20 μ l.	5 mg. 0.9 ml. 40 μ l.	5 mg. — 0.9 ml.
Percentage recovery of procaine	110	108	88	88	98

contaminated with blood and no significant metabolism of procaine in these concentrations in whole blood. Possible inactivation of the enzyme by pH changes due to the procaine HCl (which is acid) were excluded by dissolving the procaine in phosphate buffer (0.15 M) at pH 6.8 just before mixing with blood; 92 per cent of the added procaine was recovered after incubation of this mixture.

CONCLUSION

These data suggest that at clinical concentrations of procaine there is no significant metabolism of procaine in blood or cerebrospinal fluid contaminated with blood. The metabolism of procaine probably does not contribute to the failure of spinal anesthesia if there is a hemorrhagic spinal tap. It is likely, therefore, that failure to establish satisfactory anesthesia after performing a hemorrhagic spinal tap is due to other causes.

REFERENCE

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The Use of Radioiodinated Serum Albumin to Confirm Accidental Intravascular Insertion of Epidural Catheters

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Toxic reactions following epidural injection of local anesthetic agents may be due to intravascular injection, rapid absorption of normal doses, or to the administration of excessive doses. During an investigation of the use of 3 per cent meprylcaine hydrochloride (Oracaine),[†] for continuous epidural anesthesia administered through thin polyvinylite catheters, convulsions occurred in three patients. All convulsions were encountered in one group of 23 elderly patients, operated on for benign prostatic hypertrophy or prostatic cancer. The convulsions occurred during or immediately after the injection of local anesthetic agent, and were controlled by intermittent positive pressure ventilation with oxygen, and the intravenous injection of succinylcholine dichloride (Anectine) and/or thiopental sodium (Pento-

thal). No regional anesthesia developed in any of the subjects. The sequence of rapid onset of convulsions and lack of regional analgesia were suggestive of intravascular injection.

METHODS AND RESULTS

To test the validity of this assumption in two subsequent similar cases in whom convulsions developed after receiving a 3 ml. test dose followed, respectively, by 14 and 18 ml. 3 per cent meprylcaine the catheters were left *in situ*. Measured amounts, of approximately 5 μ c., radioiodinated serum albumin (RISA) were injected through the catheters, which were then flushed with 5 ml. physiological saline. At 1, 3, 5, 10, and 20 minutes after the administration of RISA, blood samples were withdrawn from an arm vein and their radioactivity measured.

In another patient, scheduled for a transurethral resection of the prostate, continuous epidural anesthesia was attempted by injection

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† All solutions of local anesthetic agents used in this study contained 1 to 200,000 epinephrine hydrochloride.

TABLE 1. RISA Percentages Reaching Peripheral Venous Blood

Case	Agent	Toxic Reaction	Percentage of RISA Demonstrable in Peripheral Venous Blood at the Times* Indicated				
			1	3	5	10	20
1	Meprylcaine	Yes	86	100	100	100	91
2	Meprylcaine	Yes	84	99	96	95	91
3	Lidocaine	Yes	16	71	77	79	76
4	Meprylcaine	No	0.3	0.0	0.5	1.3	8.7
5	Lidocaine	No	1.1	1.7	1.5	1.9	2.6
6	Lidocaine	No	0.7	0.4	1.3	2.0	4.7

* Expressed in minutes after the injection of RISA.

of a test dose of 2 ml. followed by 18 ml. of 1.5 per cent lidocaine hydrochloride (Xylocaine). Approximately 1 minute after the injection, palpitations followed by facial pallor, twitching of the extraocular and facial muscles, left ptosis and dysarthria occurred. These complications gradually subsided over the ensuing 20 minutes. No regional anesthesia developed. The catheter was left in position, and the operation was performed under general anesthesia. Postoperatively RISA was injected through the catheter and blood samples were analyzed in the manner previously described.

For comparison, RISA was injected through epidural catheters and the radioactivity of blood samples was determined in three additional patients, in whom uneventful lumbar epidural block was produced by a similar technique with either 3 per cent meprylcaine or 1.5 per cent lidocaine.

The percentage of the injected dose of RISA reaching the systemic circulation at the times of withdrawal of blood samples was initially calculated on the basis of the estimated blood volume (65 ml./kg. body weight). In the three patients in whom systemic toxic reactions occurred, blood volumes were determined the following day and the percentages of RISA reaching the circulation were then recalculated from the actual blood volumes. These results and the results obtained in the three uneventful cases are shown in table 1.

DISCUSSION AND CONCLUSION

The findings indicate that in the three cases in whom systemic toxic reactions followed the injection of a local anesthetic agent, the tip of

the catheter must have been lying in an epidural vein. In cases one and two all the RISA injected through the epidural catheters was demonstrated in the systemic circulation within three minutes. After 10 minutes the concentration of RISA declined slightly. An initial rise, plateau and fall in blood RISA concentration characteristically follows the intravenous injection of this agent.¹ The fall has been attributed to the uptake of RISA primarily by the thyroid and the liver.¹ In case 3 RISA could not be recovered quantitatively from the blood samples, and the peak concentration of 79 per cent was not reached until the tenth minute. The delayed and decreased peak concentration of RISA encountered in case 3 may be attributable to the fact that blood samples could only be obtained from a superficial forearm vein in this subject. In all other subjects blood samples were withdrawn from an antecubital vein.

In the three uneventful cases the percentage of RISA reaching the circulation ranged from 1.3 to 2.0 per cent by the tenth, and from 4.7 to 8.7 per cent by the twentieth minute after its injection. These considerable lower concentrations of RISA are in marked contrast to the corresponding values of the first three cases.

A small amount of blood stained fluid was noted only in the catheter of the third of the three patients showing toxic manifestations, and blood could not be aspirated from any of the catheters.

Bromage² encountered unusually high plasma levels of lidocaine in one patient in whom toxic signs followed the epidural injection of this agent. In this case blood was noticed in the catheter during its insertion and

no regional anesthesia developed. However, quantitative chemical determination of local anesthetic agents in blood is complex and necessary facilities are usually not available. Consequently when direct intravascular injection of a local anesthetic agent is suspected during attempted epidural block RISA may be used in the manner described to establish a diagnosis.

When systemic toxic reactions occur during or immediately following the injection of a local anesthetic agent through a catheter or needle inserted into the epidural space and regional anesthesia does not develop, intravascular injection of the anesthetic agent is the most likely cause. In three consecutive cases

it was possible to demonstrate this by the quantitative recovery of RISA, injected through epidural catheters, from samples of peripheral blood.

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Preservation of Volatile Anesthetics in Blood and Tissue

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Recent advances in the determination of anesthetic vapors in gas, blood, and tissues by means of flame ionization detection permit an analysis of samples weighing one to 20 mg. to be completed within one-half to two minutes.^{1,2} Tissue blanks do not produce any volatile organic components when heated between 100 to 120° C. At this temperature, cyclopropane, ether, chloroform, halothane, methoxyflurane, and trifluoroethyl vinyl ether are distilled, rapidly and quantitatively, into a carrier gas for analysis. Chromatography is not required when any one of these agents is employed as the sole volatile anesthetic agent; and tedious tissue extractions are avoided.

The techniques developed for the collection and preservation of the anesthetic levels in tissues should be of particular interest to clinical anesthesiologists, pathologists, pharmacologists, and toxicologists. The methods provide a convenient means for mailing specimens to laboratories specializing in these determinations.

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METHOD

Ordinary core solder (1.5 mm. inside diameter, 3.12 mm. outside diameter) was purchased from a hardware store in the form of one-pound spools. Without removing the solder from the spool, the two ends were opened by scratching deeply with a file and flexing until a clean break was obtained. The loose or free end was attached to a vacuum source and the entire spool was submerged in hot water to remove the zinc chloride flux. The tubing was rinsed several times with distilled water and sucked dry with air. The internal volume was approximately 0.05 ml. (50 μ l. or 50 mg.) per inch of length and could be broken off to any desired length.

Tissue specimens obtained during operation, autopsy or animal experimentation were inserted into 1 ml. disposable polyethylene tuberculin syringes with a minimum of exposure. The rubber tipped plunger was covered with a small square of Saran Wrap † and inserted into the barrel behind the tissue. The plunger was advanced until the tissue reached

† Dow Chemical Company, Midland, Michigan.