

Distribution of Catheter-injected Local Anesthetic in a Model of the Subarachnoid Space

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Maldistribution of local anesthetic administered through a subarachnoid catheter recently has been implicated as a possible cause of sacral root injury. To examine subarachnoid distribution of catheter-injected local anesthetic, we constructed a model of the subarachnoid space and administered solutions containing lidocaine and methylene blue through sacrally directed catheters. We studied three catheters: a 28-G endport, a 20-G endport, and a 20-G multiple sideport. To determine the injection rates to be used, ten clinicians were observed while they performed mock subarachnoid injections: the mean (\pm standard deviation) "normal" injection times for the 28-G and 20-G catheters were 52.6 ± 17.2 and 11.9 ± 7.2 s, respectively. The correlation coefficient for lidocaine concentration estimated by methylene blue spectrophotometric absorbance and measured by immunoassay was 0.977. Administration of hyperbaric local anesthetic through a sacrally directed catheter resulted in restricted distribution of anesthetic with a relatively high peak concentration. Rate of injection was a critical factor affecting distribution; faster injections tended to distribute solution more uniformly and to a higher segmental level, resulting in substantially lower peak concentrations. When catheters were injected at clinically relevant rates, the 28-G catheter produced the greatest degree of maldistribution; this difference appeared to be primarily a function of flow rate. Differences in peak lidocaine concentration between the two 20-G catheters were neither large nor consistent. However, despite sacral placement, the multiple-sideport catheter distributed anesthetic toward "higher" spinal segments more consistently. Distribution was more favorable when the injected solution was less dense (closer to isobaric). We conclude that administration of hyperbaric local anesthetic through a sacrally directed catheter results in a restricted distribution and a high peak local anesthetic concentration. Several factors can affect distribution, including catheter size, tip configuration, tip position, injection rate, and baricity of local anesthetic solution. (Key words: Anesthetic techniques, spinal: continuous. Anesthetics, local: lidocaine. Complications, neurologic: cauda equina syndrome.)

RECENTLY, WE DESCRIBED four cases of cauda equina syndrome that occurred after continuous spinal anesthesia.¹ All of these cases had in common the administration of a dose of local anesthetic that was greater than that usually administered using a single-injection technique; these relatively high doses had been administered incrementally to extend a predominantly sacral block to

achieve adequate surgical analgesia. Because of this common element, we postulated that these deficits resulted from maldistribution of local anesthetic, incurring a direct neurotoxic effect of the anesthetic.

The probability that neurotoxic damage will occur is directly related to the concentration of local anesthetic to which neural tissue is exposed.²⁻⁴ Relatively high localized concentrations could result if anesthetic administered into the subarachnoid space were to distribute in a nonuniform or restricted fashion. Nonuniform distribution of local anesthetic in the sacral portion of the subarachnoid space would be reflected clinically by a "low" or patchy block; all four of the reported cases of cauda equina syndrome shared this common element.

The present studies were conducted to examine the distribution of local anesthetic within a model of the subarachnoid space when the anesthetic is administered through a catheter. The purpose was to identify factors that might favor a restricted sacral distribution and thereby result in a relatively greater concentration of local anesthetic within the sacral portion of the subarachnoid space. In addition, we sought to determine the value of methylene blue for quantifying anesthetic distribution.

Materials and Methods

A model of the subarachnoid space was constructed from an acrylic tube (inner diameter, 1.8 cm; outer diameter, 2.5 cm). The distal 5 cm of the tube was machined to approximate the sacral taper of the subarachnoid space. The shape and dimensions of the model were developed from lateral magnetic resonance imaging scans of the spines of adult men. Sampling ports were placed at 2-cm intervals along the "ventral" surface of the plastic tube; one additional sampling port was placed at the sacral end of the model. Sampling ports were correlated with a particular vertebral body interspace by referring to the magnetic resonance imaging scans (e.g., ports 1, 4, and 8 approximated S2-S3, L3-L4, and T10-T11, respectively). A single injection port at approximately L3-L4 was placed on the "dorsal" surface at the peak of the lumbar lordosis.

The model was filled with an artificial cerebrospinal fluid (CSF) of pH 7.4-7.6, specific gravity 1.004, and ionic composition similar to CSF: sodium 140-150 mEq/l, chloride 120-130 mEq/l, albumin 25 mg%, and glucose 50 mg%. The solution used for all injections (except experiment 3) was a 20:1 mixture of 5% lidocaine hydrochloride with 7.5% glucose (Astra Pharmaceutical, West-

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boro, MA) and 1% methylene blue solution (American Regent Laboratories, Shirley, NY); this mixture yielded a hyperbaric solution with an effective concentration of 4.76% lidocaine hydrochloride and a specific gravity of 1.047. In experiment 3, the solution was a 20:1 mixture of 2% lidocaine hydrochloride (Elkins-Sinn, Cherry Hill, NJ) and 1% methylene blue; this mixture yielded a solution with effective concentration of 1.9% lidocaine hydrochloride and a specific gravity of 1.014.

To determine the injection rates to be used for the model studies, we observed 10 anesthesiologists (5 attending physicians and 5 residents) while each performed a mock spinal anesthetic using a 20-G multiple-sideport catheter (Kendall Healthcare, Mansfield, MA), a 28-G endport catheter (CoSpan®, Kendall Healthcare), and a 25-G spinal needle (Monoject®, Sherwood Medical, St. Louis, MO). Subjects were not informed of the specific aspect of continuous spinal anesthesia being observed. First, each was asked to place the appropriate needle through a rubber block, place the catheter, and then inject 1 ml fluid through the catheter as though administering an anesthetic to a patient ("normal" injection). Next, each was asked to inject 1 ml fluid through each catheter as rapidly as each believed acceptable in a clinical setting ("fast" injection). Finally, each was asked to inject 1 ml fluid as rapidly as possible ("maximum" injection). The exercise was videotaped; after the exercise was completed, the videotape was reviewed to determine the mean rate for each type of injection. These results were used to select the injection rates for experiment 1.

All injections were performed using an angiography infusion pump (Mark IV CT Contrast Injector, Medrad, Pittsburgh, PA) modified to hold a 1-ml syringe. The

pump can generate 300 psi which, when coupled with the use of a 1-ml syringe, can maintain high flow rates, even through high-resistance catheters. The model was leveled and maintained in a horizontal position during all injections. Beginning 3 min after each injection, 0.3-ml samples of CSF were aspirated from eight different sample ports *via* 25-G needles; each needle was placed through the sampling port and positioned with its tip at the lower inner surface of the model. Starting at the sacral end, samples were obtained from every other sampling port (*i.e.*, 4 cm apart, ranging from sacral to thoracic segments). The absorbance of each sample was measured spectrophotometrically (model 240, Gilford Instrument Laboratories, Oberlin, OH) at 675 nm and compared with the absorbance of the injected local anesthetic mixture to yield a fraction of the injected concentration. This fraction was used to estimate the lidocaine concentration of the sample. For experiments 1 and 2, the sample with the highest estimated concentration was assayed for lidocaine using a homogeneous enzyme immunoassay technique (Emit®, Syntex, Palo Alto, CA). The estimated and assayed lidocaine concentrations were compared using simple linear regression; a correlation coefficient was calculated using the least-squares method.

EXPERIMENT 1

We studied three catheters: a 20-G endport, a 20-G multiple sideport, and a 28-G endport catheter (all Kendall Healthcare, Mansfield, MA) (figs. 1 and 2). For each injection, the selected catheter was passed through the injection port in a sacral direction and advanced 3.5 cm into the model. One set of injections was completed with

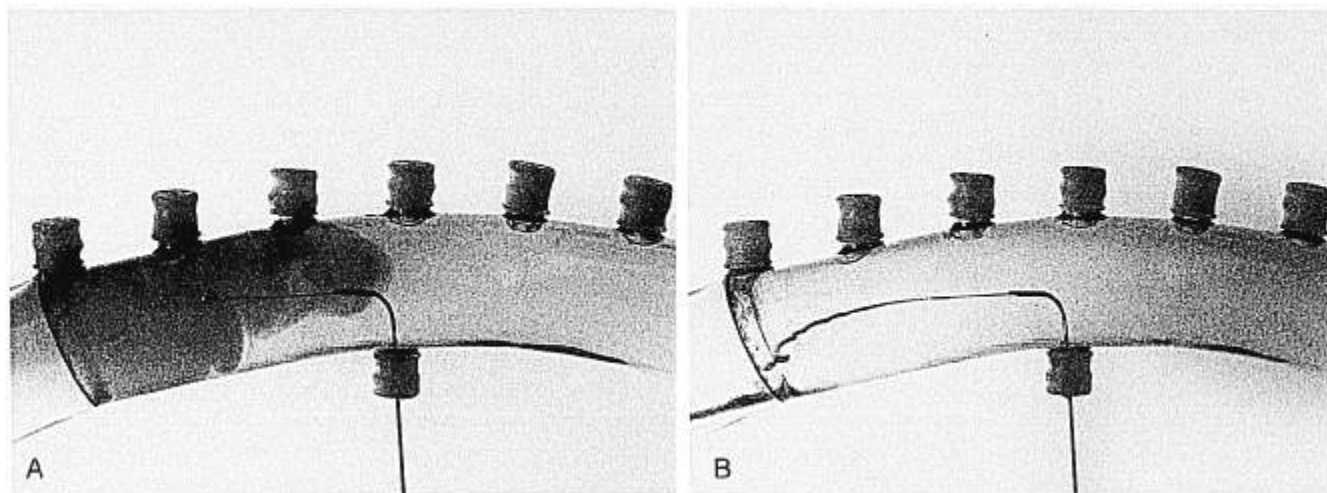


FIG. 1. Injection of 1 ml lidocaine/dye mixture *via* a centrally placed 28-G endport catheter at 10 s (A) and 90 s (B). The catheter is directed toward the sacral end of the model. The 10-s injection tends to disperse the solution and promote rapid dilution. In contrast, the 90-s injection creates a small stream with little turbulence and produces a thin dense layer of dye at the bottom of the spinal model.

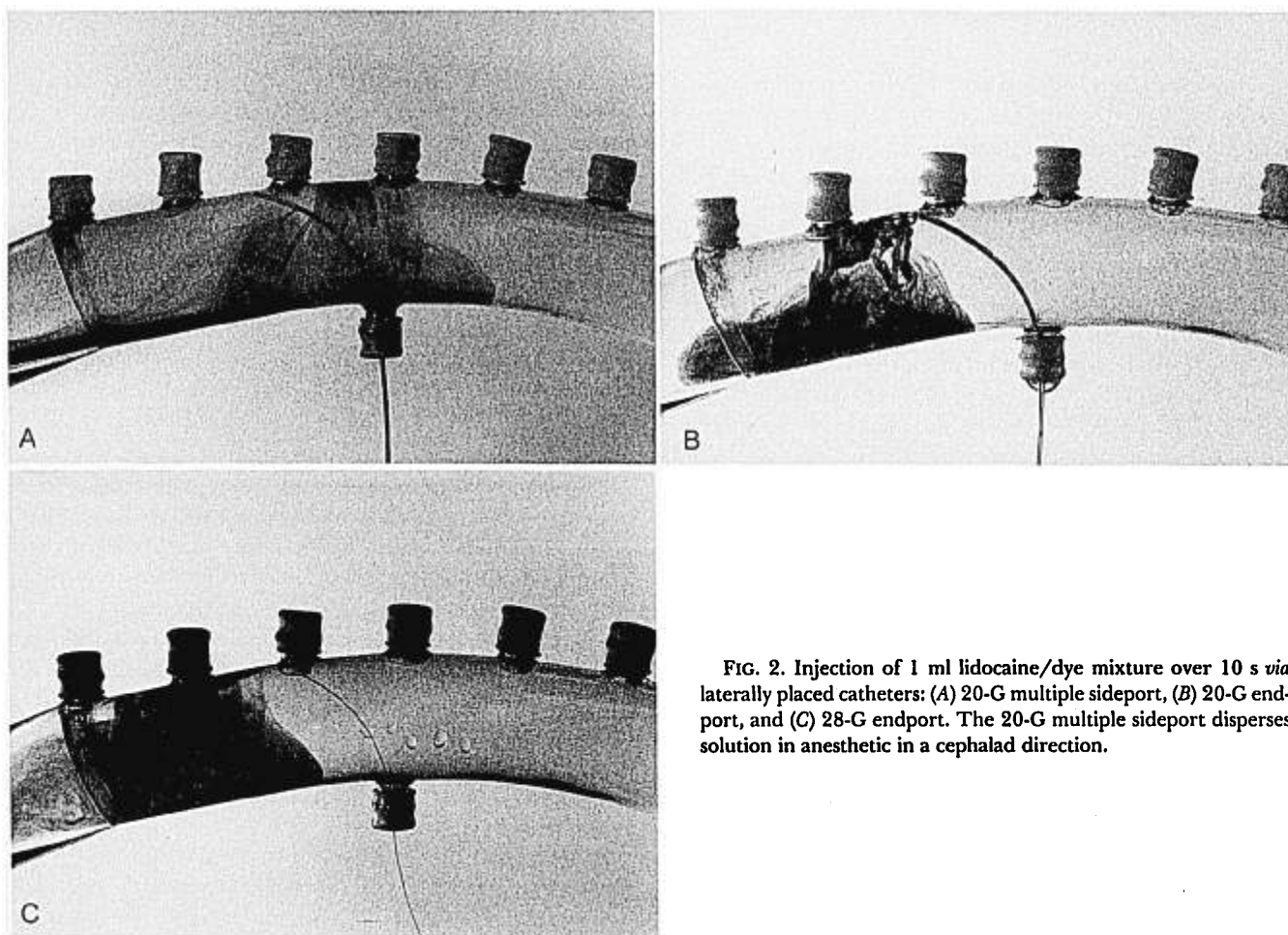


FIG. 2. Injection of 1 ml lidocaine/dye mixture over 10 s via laterally placed catheters: (A) 20-G multiple sideport, (B) 20-G endport, and (C) 28-G endport. The 20-G multiple sideport disperses solution in anesthetic in a cephalad direction.

the tip of the catheter pointed sacrally and resting against the "ventral" surface of the model ("lateral" placement). A second set of injections was completed with the tip of the catheter positioned equidistant from and parallel to the lateral walls of the model ("central" placement). One ml of the anesthetic-methylene blue mixture was injected through the 20-G endport and multiple-sideport catheters in each position (lateral and central) over 5, 10, and 20 s. One milliliter was injected through the 28-G endport catheter in each position over 10, 20, 30, 45, 60, and 90 s. Finally, a 25-G spinal needle (Monoject) was passed 1 cm through the injection port, and 1 ml of the anesthetic-dye mixture injected over 10 s (fig. 3).

EXPERIMENT 2

With the 28-G endport catheter in central position, three sequential 1-ml injections (each over 60 s) of the anesthetic-dye mixture were administered. The injections were spaced 5 min apart, and the model was not disturbed between injections. Three min after the completion of

the third injection, CSF samples were obtained and measured as previously described.

EXPERIMENT 3

One milliliter of the 1.9% lidocaine-dye solution was injected through a 28-G catheter in a central position over 90 s. Three minutes after the completion of the injection, CSF was sampled from the "lower" inner surface of the model, and methylene blue absorbance was measured. The experiment was repeated, but in the second trial, the set of samples was aspirated from the "middle" of the model (the point midway between the upper and lower inner surface). The methylene blue absorbance of each set was measured and compared with injectate absorbance as described in experiment 1.

Results

The time to inject 1 ml of fluid through either the 20-G catheter or the 25-G spinal needle was shorter than

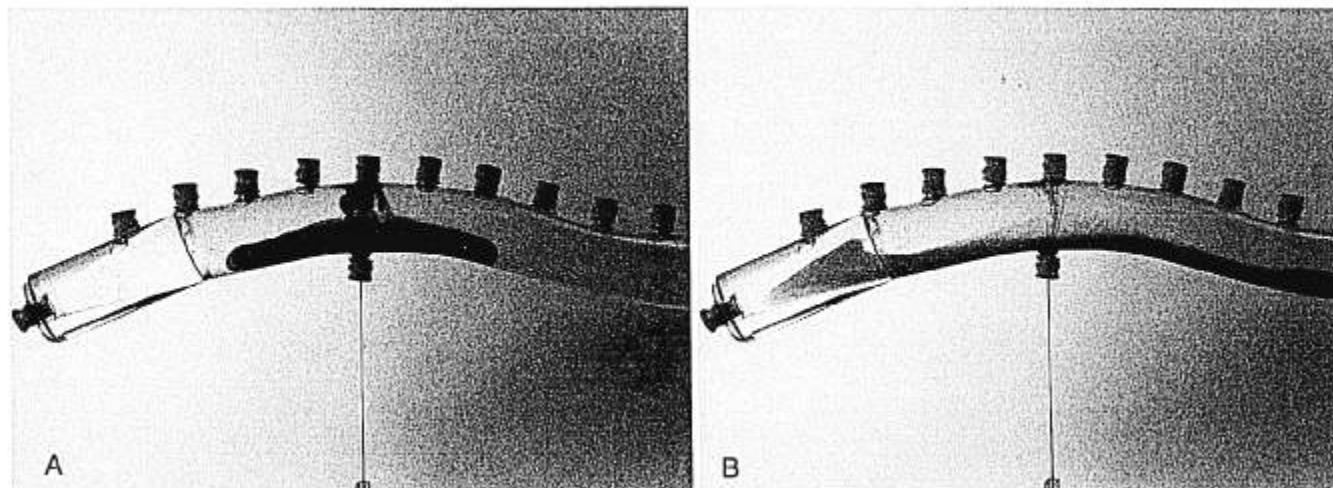


FIG. 3. Injection of 1 ml lidocaine/dye solution over 10 s through a 25-G spinal needle (A: during injection; B: immediately afterward). The stream of anesthetic is directed toward the ventral wall of the model, facilitating mixing; the needle's position near the peak of the lumbosacral curve encourages movement of solution in both cephalad and caudad directions.

that for the 28-G catheter (fig. 4). The mean normal injection time for the 20-G catheter was 11.9 ± 7.2 s (mean \pm standard deviation), for a 25-G spinal needle was 9.8 ± 2.6 s, and for the 28-G catheter was 52.6 ± 17.2 s. The fast and maximum injection times also differed; again, the use of the larger catheter resulted in shorter injection times. The mean fast and maximum injection times for the 20-G catheter were 3.0 ± 1.1 and 1.3 ± 0.7 s, respectively, and for the 28-G catheter, 27.5 ± 5.2 and 17.3 ± 3.2 s, respectively.

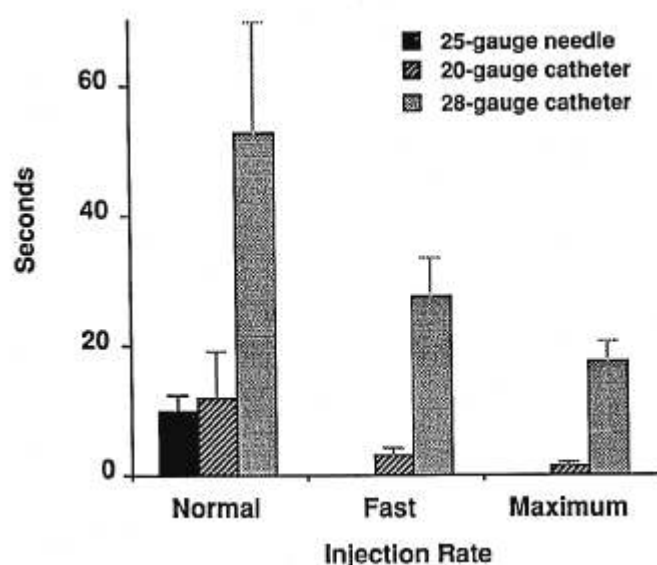


FIG. 4. Mean (\pm SD) time taken by clinicians to inject 1 ml fluid through a 28-G catheter, a 20-G catheter, and a 25-G spinal needle ($n = 10$).

EXPERIMENT 1

All catheters distributed dye predominantly in a sacral pattern (fig. 5). The peak absorbance of methylene blue in all injections always was greatest in the sample aspirated from the most sacral port of the model. In general, the magnitude of this peak absorbance varied inversely with injection rate.

The measured peak lidocaine concentrations are shown in table 1. The correlation coefficient for lidocaine concentration estimated by the fraction of injected absorbance and that measured by immunoassay was 0.977.

The distribution of lidocaine-dye mixture with the 25-G spinal needle is depicted in figure 6. Peak dye absorbance was at the most sacral port.

EXPERIMENT II

The pattern of distribution after three sequential 1-ml injections of lidocaine-dye mixture was similar to that after a single 1-ml injection. However, the magnitude of the peak fraction of injected methylene blue absorbance and peak measured lidocaine concentration was nearly twice that of the single injection (fig. 7).

EXPERIMENT 3

Samples obtained after injection of a more isobaric solution had lower peak fractional methylene blue absorbances than samples obtained with a denser solution (experiments 1 and 2). Peak dye absorbance was again at the most sacral port, but the pattern of dye distribution was more uniform (fig. 8).

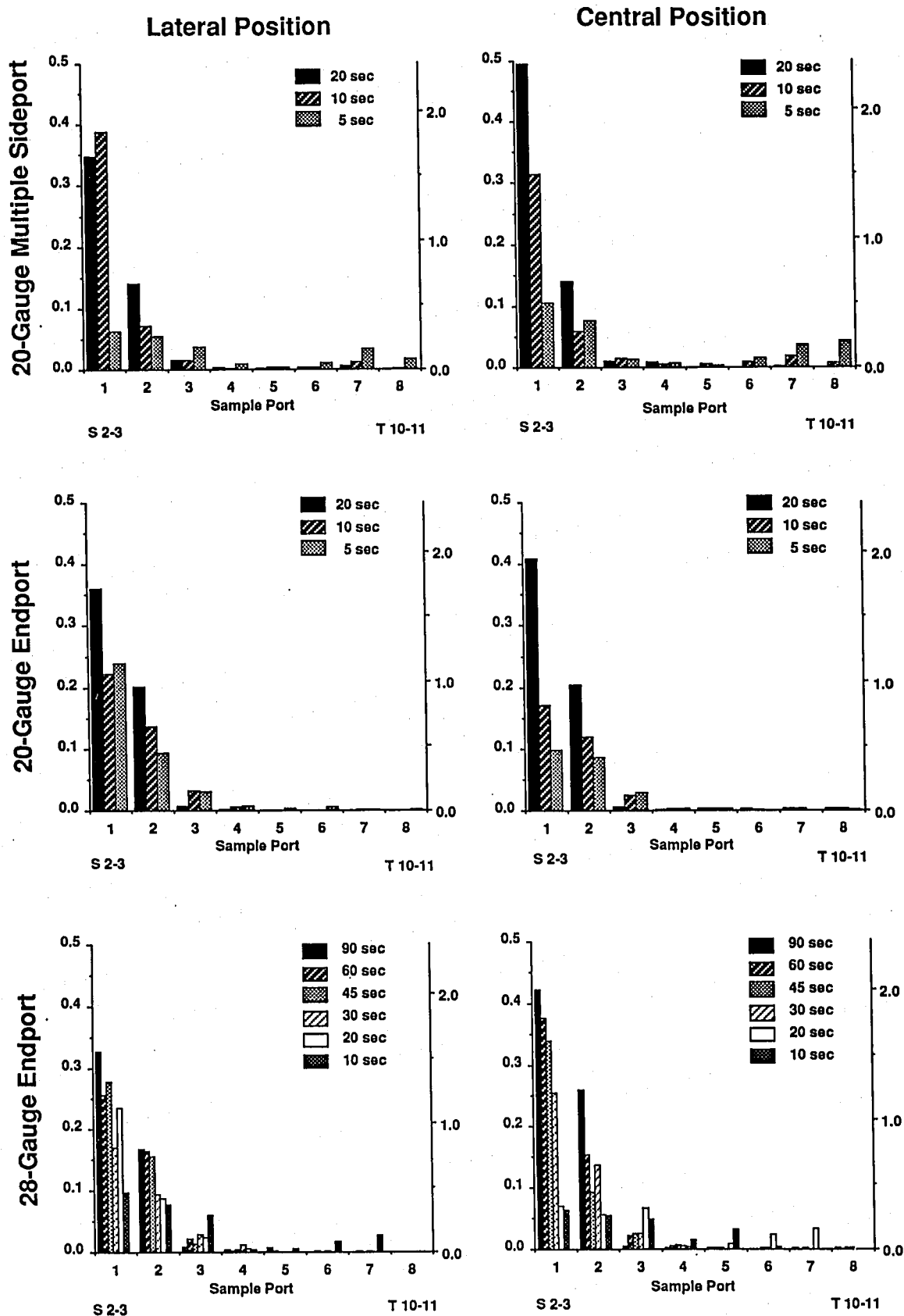


FIG. 5. Effect of injection rate on distribution of 1 ml lidocaine/dye mixture (4.76% lidocaine hydrochloride). All injections were made *via* catheters directed sacally, placed in either a lateral or central position. S2-S3 and T10-T11 identify the approximate vertebral interspaces of sampling ports 1 and 8, respectively.

TABLE 1. Measured Lidocaine Concentration

Catheter	Injection Rate (s)	Lidocaine Concentration (%)	
		Catheter Position	
		Lateral	Central
20-G multiple sideport	20	1.53	2.39
	10	1.92	1.53
	5	0.25	0.42
20-G endport	20	1.27	2.26
	10	0.83	0.71
	5	1.07	0.42
28-G endport	90	1.59	2.16
	60	0.94	1.43
	45	1.12	1.22
	30	0.61	1.27
	20	0.96	0.26
	10	0.38	0.22

Measured lidocaine concentration from sample with peak methylene blue absorbance after injection of 1 ml 4.76% lidocaine hydrochloride/methylene blue solution.

Discussion

Our results demonstrate that administration of hyperbaric local anesthetic through a sacally directed catheter results in a restricted distribution of anesthetic. Similarly, recently published photographs from a qualitative model study depict a restricted spread of dye after injection of hyperbaric solution from a sacally directed catheter.⁵

Our data show that a sacally restricted distribution results in a relatively high peak concentration of anesthetic. Similar high anesthetic concentrations were obtained in a clinical study by Mörch *et al.*,⁶ who measured CSF concentrations of lidocaine after injection of the local

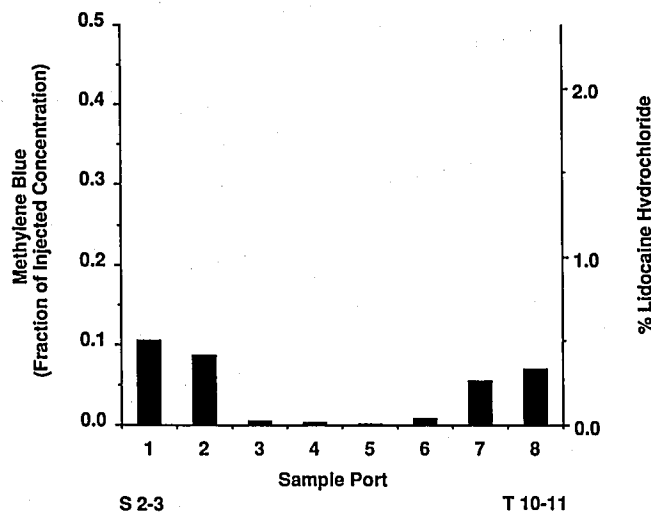


FIG. 6. Distribution of 1 ml methylene blue/lidocaine mixture injected over 10 s through a 25-G spinal needle. Injection was performed with the model in a "supine" position.

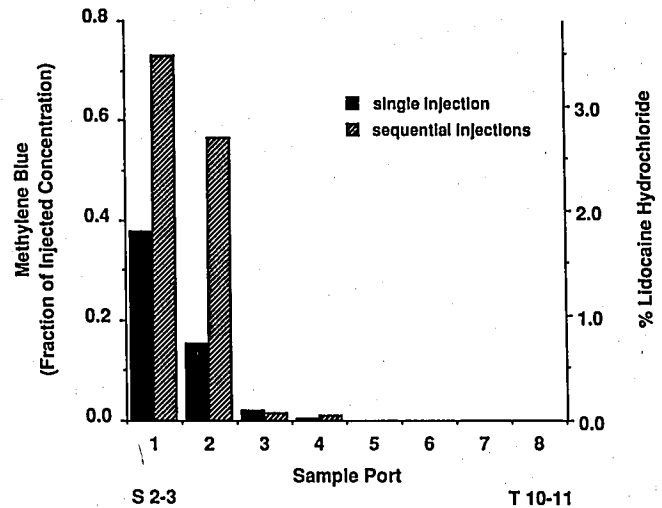


FIG. 7. Effect of three sequential injections on distribution of the lidocaine/dye mixture. Two experiments are compared. In the first, 1 ml lidocaine/dye mixture (4.76% lidocaine hydrochloride) was injected over 60 s; in the second, three sequential 1-ml injections (5 min apart) were made with the catheter in the same fixed position.

anesthetic through subarachnoid catheters. In one patient, the tip of the catheter was unintentionally positioned in the sacral area; the CSF concentration of lidocaine aspirated 15 min after injection was almost nine times greater than the mean concentration aspirated from catheters appropriately placed in a cephalad position.⁶

Rate of injection was a critical factor affecting distribution in our model. Although all sacally directed cath-

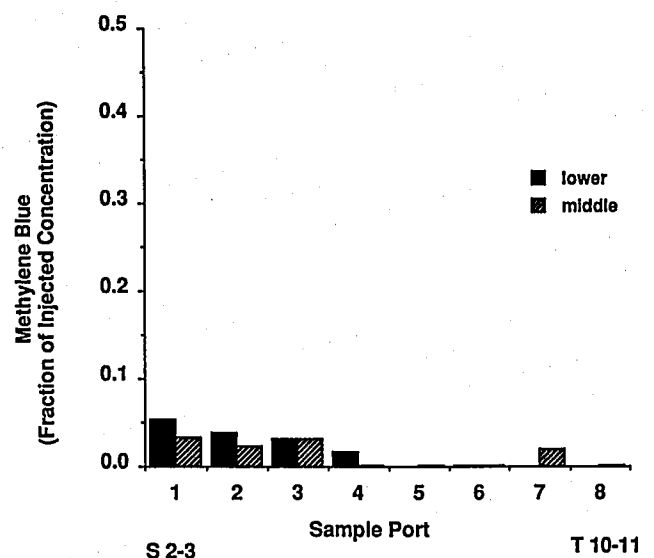


FIG. 8. Distribution of 1 ml 1.9% lidocaine/dye mixture injected through a 28-G catheter in a central position over 90 s. "Lower" samples are aspirated from the base of the model; "middle" samples are aspirated from the center of the model.

eters produced peak concentrations of lidocaine at the most sacral port, faster injections tended to distribute solution more uniformly and to a higher "segmental" level, resulting in substantially lesser peak concentrations. For example, when injected *via* a centrally placed 20-G multiple-sideport catheter, the concentration of lidocaine in the sacral end of the model ranged from 0.42% (5-s injection) to 2.39% (20-s injection).

It is our clinical impression that maldistribution occurs more frequently when a microcatheter is used for continuous spinal anesthesia. The results of the present experiments suggest that this tendency of a small catheter to maldistribute anesthetic is primarily a function of flow rate. For example, our clinicians' "normal" rate of injection through a 28-G catheter was much slower than that through a 20-G catheter, suggesting that the 28-G catheter will produce a more restricted block. However, if solution is injected rapidly through a small catheter, distribution does become more uniform (figs. 1 and 5). In fact, when injections were made at identical rates (either 10 or 20 s), the 28-G microcatheter actually distributed anesthetic more uniformly than did either of the two larger catheters (fig. 9). One explanation for this finding may be that the higher velocity stream of the small catheter promotes mixing of the two solutions.

Maldistribution also will occur if a slow injection is made through a large (20-G) catheter. However, injections through large catheters typically are fast (*i.e.*, the mean "normal" rate of injection was 11.9 s), and even more rapid injections are easily performed (*e.g.*, the average "fast" injection was 3 s). In contrast, a rate of injection through a 28-G catheter that produces a relatively uniform distribution is one that few clinicians can *physically* accomplish. None of our clinicians could inject 1 ml in less than 13.5 s; a rate of 10 s was achieved in these experiments by modifying a high-pressure angiography infusion pump. One obvious solution is to use small-bore catheters of much shorter length; whether this solution is practical remains to be determined.

Injection rate generally has been considered only a minor determinant of local anesthetic distribution,⁷ primarily because most studies have examined only rates that are clinically relevant for injections through a needle (*e.g.*, 1 ml/s to 1 ml/10 s)^{8,9} and not through a catheter. Although rarely performed, slow injections through a needle may affect distribution. A recent study compared hypobaric tetracaine injected at 0.02 and 0.5 ml/s through a Whitacre needle and found that the slower injection produced a lower level and longer duration of anesthesia.¹⁰

Subarachnoid catheters usually are inserted to a depth greater than the anterior-posterior diameter of the space¹¹; thus, they must advance caudad or cephalad. Cephalad placement occurs more often, at least when a larger "epidural" catheter is used: most clinicians use a

Methylene Blue (Fraction of Injected Concentration)

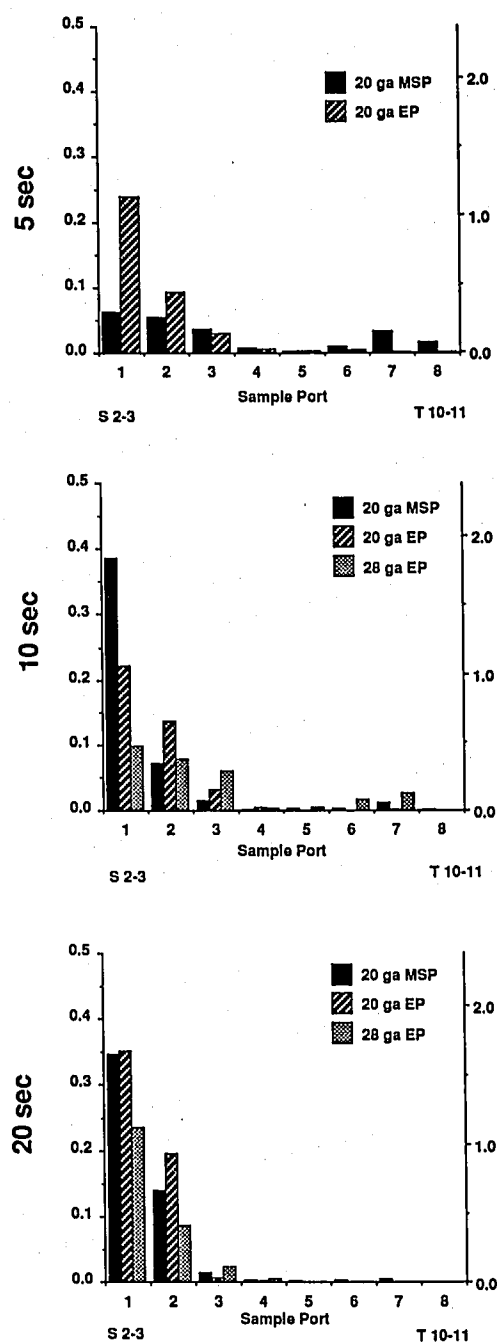


FIG. 9. Effect of catheter size and tip configuration on distribution of the lidocaine/dye mixture.

Tuohy needle with the bevel directed cranially, and the angulation of the needle favors a cephalad tip placement. However, unintentional sacral placement commonly occurs. Bridenbaugh *et al.*¹² radiographically examined the position of subarachnoid catheters in 209 patients: 43 (21%) of the catheters ended in a loop, and 24 (11%) were coiled at the insertion site.¹² Sacral placement of a subarachnoid catheter tip may be more frequent when a mi-

croatheter is used because a straight spinal needle generally is used for placement, and the small size and flexibility of the catheter may increase the likelihood of sacral deflection.

If a catheter is positioned sacrally and anesthetic is injected slowly, neural tissue may be exposed to relatively high concentrations of local anesthetic (*e.g.*, 2–3% after a single injection of 50 mg 5% lidocaine hydrochloride). Numerous animal studies have shown local anesthetics to be capable of causing neurotoxic damage when administered in large doses or excessive concentrations.^{2–4,13–15} In addition to concentration and dose, a number of other factors may affect the potential for neurotoxic damage; these include duration of exposure, type of anesthetic, nerve fiber diameter and degree of myelination, and microenvironmental factors such as CSF pH.^{16–18}

A restricted sacral distribution will result in little, if any, anesthetic reaching the “higher” spinal segments. In the study by Mörch *et al.*, the one patient in whom the catheter had been positioned sacrally developed a “low” block and required general anesthesia.⁶ A restricted sacral distribution may explain the apparent lack of anesthesia in a report of two failed continuous spinal anesthetics.¹⁹ It is noteworthy that in both cases the catheter had been advanced in a caudad direction. Few clinicians routinely test for a block by a careful examination of the sacral dermatomes, and thus a restricted distribution may be misinterpreted as a complete failure of the technique.

The potential harm from maldistribution of an initial injection of local anesthetic can be compounded by ensuing clinical decisions. If the sensory level achieved is not sufficient for the planned surgery, additional doses of local anesthetic may be administered. The concentration of local anesthetic in the sacral area becomes even greater while sensory blockade may climb very slowly. Unlike the repeated single-injection technique, an indwelling catheter in a relatively fixed position distributes local anesthetic in the same pattern, reinforcing the areas that already have the highest concentration. Experiment 2 demonstrates the consequences of this sequence of events (fig. 7).

Injection of local anesthetic solution through a 25-G spinal needle produced a relatively uniform distribution with a low peak concentration (fig. 6). Favorable distribution is apparently encouraged by three factors: 1) a relatively fast injection rate (10-s injection); 2) the needle is directed perpendicular to the long axis of the subarachnoid space, directing the stream of anesthetic toward the ventral wall of the model and thereby facilitating mixing with the CSF; and 3) the needle is positioned near the peak of the lumbosacral curve, encouraging movement of solution in both a cephalad and a caudad direction. It should be noted that this injection was performed with the model in a “supine–horizontal position.” Although

there are examples of needle injections performed with patients in this position (*e.g.*, Lemmon’s split-mattress technique for continuous spinal anesthesia²⁰), they are quite rare. Most spinal injections are performed with the patient seated or in lateral decubitus. Obviously, distribution will be profoundly affected by these differences in positioning and by movement of the patient after injection.

Catheter configuration (number and position of the ports of a catheter) also may influence distribution of local anesthetic. This study compared catheters with two different configurations—single endport and multiple sideport. The latter has a closed tip and three radial ports, each of which directs a stream slightly toward the tip of the catheter. At identical injection rates, differences in peak lidocaine concentration between the two 20-G catheters were neither large nor consistent (table 1). However, the multiple-sideport catheter distributed anesthetic toward “higher” spinal segments more consistently, even at the slower injection rates. This may, in some cases, prevent the need for a repeated injection to achieve adequate analgesia. Alternatively, because a sacrally placed multiple sideport catheter may produce some sensory block at “higher” dermatomes, sacral placement may be more difficult to detect than with an endport catheter. Thus, this failure to easily detect sacral placement could actually be a disadvantage. In either case, if a catheter produces a sacrally restricted or patchy block after a reasonable initial dose, consideration should be given to maneuvers such as changing patient position, altering lumbosacral curvature, or switching to a different baricity of local anesthetic, and to replacing or repositioning the catheter. If these maneuvers fail to provide well-distributed anesthesia, the technique should be abandoned.

Distribution can be improved by using a solution that is closer to isobaric (fig. 8). Injection of a solution with a specific gravity of 1.014 (2% lidocaine–methylene blue) over 90 s through a centrally placed 28-G catheter produced a more favorable distribution than the comparable injection of 5% lidocaine mixture with a specific gravity of 1.047. That is, distribution of solution was far more uniform, and although the peak concentration still occurred at the most sacral port, the magnitude of the peak was far less than that for the more hyperbaric injection.

This study has several limitations. The model contained no spinal cord. However, all injections were performed with catheters directed sacrally, and although nerve roots may have some effect on distribution, they are unlikely to alter it substantially. Physiologic factors that may disperse local anesthetic such as CSF circulation and arterial pulsations were absent from the model. However, flow of CSF into the caudal portion of the subarachnoid space has been estimated to be less than 10% of the 500 ml produced daily,⁷ and arterial pulsations are minimal in

the caudal portion of the subarachnoid space. Although there was neither uptake nor elimination of local anesthetic in the model, their effect on anesthetic concentration is likely to be far less important in the first few minutes after injection than the physical factors that are present.

An important finding in the present study is the close correlation between methylene blue spectrophotometric absorbance and measured lidocaine concentration. Methylene blue often has been used to demonstrate gross movement of local anesthetic in models²¹; our results indicate that it can be used as a quantitative method as well, at least within the first few minutes after injection of hyperbaric local anesthetic. That the actual concentration of lidocaine in the one sample aspirated 21 min after the start of the first injection (experiment 2) was very close to that predicted by absorbance suggests that methylene blue distribution may continue to reflect lidocaine distribution for a longer period.

In summary, we have shown that administration of local anesthetic through a sacrally directed catheter results in a restricted distribution with a relatively high peak local anesthetic concentration, and with little, if any, anesthetic reaching higher spinal segments. This pattern of distribution could result in neurotoxic injury, particularly if additional anesthetic is administered to achieve an adequate sensory block. Factors that can affect distribution include catheter diameter, tip position, tip configuration, injection rate, and baricity of local anesthetic solution. Of these, injection rate appears to be the most critical, with high rates (5–10 s) distributing local anesthetic more uniformly.

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References

1. Rigler M, Drasner K, Krejcie T, Yelich S, Scholnick F, DeFontes J, Bohner D: Cauda equina syndrome after continuous spinal anesthesia. *Anesth Analg* 72:275–81, 1991
2. Adams HJ, Matri AR, Eicholzer AW, Kilpatrick G: Morphologic effects of intrathecal etidocaine and tetracaine on the rabbit spinal cord. *Anesth Analg* 53:904–908, 1974
3. Kalichman M, Powell HC, Myers RR: Quantitative histologic analysis of local anesthetic-induced injury to rat sciatic nerve. *J Pharmacol Exp Ther* 250:406–413, 1989
4. Ready LB: Neurotoxicity of intrathecal local anesthetics in rabbits. *ANESTHESIOLOGY* 63:364–370, 1985
5. Lambert DH, Hurley RJ: Cauda equina syndrome and continuous spinal anesthesia. *Anesth Analg* 72:817–819, 1991
6. Mörch ET, Rosenberg MK, Truant AT: Lidocaine for spinal anaesthesia. A study of the concentration in the spinal fluid. *Acta Anaesthesiol Scand* 1:105–115, 1957
7. Greene N: Distribution of local anesthetic solutions within the subarachnoid space. *Anesth Analg* 64:715–730, 1985
8. McClure J, Brown D, Wildsmith J: Effect of injected volume and speed of injection on the spread of spinal anaesthesia with isobaric amethocaine. *Br J Anaesth* 54:917–920, 1982
9. Neigh J, Kane P, Smith T: Effects of speed and direction of injection on the level and duration of spinal anesthesia. *Anesth Analg* 49:912–918, 1970
10. Atchison S, Wedel D, Wilson P: Effect of injection rate on level and duration of hypobaric spinal anesthesia. *Anesth Analg* 69:496–500, 1989
11. Lusted L, Keats T: The skeletal system, *Atlas of Roentgenographic Measurement*. Chicago, Yearbook, 1978, pp 113–143
12. Bridenbaugh L, Moore D, Bagdi P, Bridenbaugh P: The position of plastic tubing in continuous-block techniques: An x-ray study of 552 patients. *ANESTHESIOLOGY* 29:1047–1049, 1968
13. Rosen M, Baysinger C, Shnider S, Dailey P, Norton M, Curtis J, Collins M, Davis R: Evaluation of neurotoxicity after subarachnoid injection of large volumes of local anesthetic solution. *Anesth Analg* 62:802–808, 1983
14. Pizzolato P, Rengar OJ: Histopathologic effects of long exposure to local anesthetics on peripheral nerves. *Anesth Analg* 38:138–141, 1959
15. Kalichman MW, Powell HC, Myers RR: Pathology of local anesthetic-induced nerve injury. *Acta Neuropathol* 75:583–589, 1988
16. Kalichman MW: Selective vulnerability of unmyelinated fiber Schwann cells in nerves exposed to local anesthetics. *Lab Invest* 59:271–280, 1988
17. Covino BG: Toxicity of local anesthetic agents. *Acta Anaesthesiol Belg* 39:159–164, 1988
18. Ravindran RS: Prolonged neural blockade following regional anesthesia with 2-chloroprocaine. *Anesth Analg* 59:447–454, 1980
19. Weiskopf RB: Unexplained failure of a continuous spinal anesthetic. *ANESTHESIOLOGY* 114–116, 1970
20. Lemmon WT, Paschal GW: Continuous-serial, fractional, controllable intermittent-spinal anesthesia, with observations on 1000 cases. *Surg Gynecol Obstet* 74:948–956, 1942
21. Barker A: Clinical experiences with spinal anesthesia in 100 cases. *Br Med J* 1:665–674, 1907