3 ml of 1.5 per cent lidocaine (45 mg) might produce definite signs of spinal anesthesia within two minutes. Mepivacaine in 1.5 per cent concentration is apparently ineffective as a spinal anesthetic whereas higher concentrations are effective.[5] Similarly, lidocaine normally is used in a concentration of at least 5 per cent for intrathecal use and therefore, 1.5 per cent might not produce significant spinal anesthesia within two minutes.[6]

Thus, it would seem that 3 ml of 0.75 per cent bupivacaine or 3 per cent chloroprocaine both with epinephrine 1:200,000 should provide clinical evidence of either an intravascular or intrathecal injection within two minutes. But 3 ml of 1.5 per cent lidocaine or mepivacaine both with epinephrine 1:200,000 could provide evidence of an intravascular but possibly not an intrathecal injection.

Perhaps the intrathecal injection of small volumes of these local anesthetic solutions should be specifically studied.

D. H. MORISON, M.B., CH.B., F.R.C.P.(C)
Associate Professor of Anaesthesia
McMaster University
Hamilton, Ontario L8N 3Z5

REFERENCES

1. Moore DC, Batra MS: The components of an effective test dose prior to epidural block. ANESTHESIOLOGY 55:693–696, 1981
2. Foldes FF, McNall PG: 2-chloroprocaine: A new local anesthetic agent. ANESTHESIOLOGY 13:287–296, 1952
3. Moore DC: Spinal anesthesia: Bupivacaine compared with tetracaine. Anesth Analg (Cleve) 59:743–750, 1980
4. Fargas-Babjak A, McChesney J, Morison DH: The efficacy of bupivacaine 0.75 per cent as an epidural test dose. Can Anaesth Soc J 27:500–501, 1980
5. Poe MF, Dornette WHL, Johnson CH: Clinical observations on the intrathecal use of mepivacaine. ANESTHESIOLOGY 23:678–681, 1962
6. Scott DB, Cousins MJ: Clinical pharmacology of local anesthetic agents, Neural Blockade in Clinical Anesthesia and Management of Pain. Edited by Cousins MJ, Bridenbaugh PO. Philadelphia/Toronto, JB Lippincott Company, 1980, p 92

(Accepted for publication February 23, 1982.)

Anesthesiology
57:141–142, 1982

In reply:—Morison's two primary concerns are: 1) doses of 90 mg of chloroprocaine and 22.5 mg of bupivacaine "might" result in high or total subarachnoid block; and 2) 45 mg of either lidocaine or mepivacaine "might" not produce significant spinal anesthesia in two minutes.

Whether high or total spinal block results from the unintentional injection of a local anesthetic drug depends on many factors other than dosage, *e.g.*, baricity of the solution, position of the patient, intra-abdominal pressure (obesity, pregnancy, *etc*), height, and so forth. Regardless of these, 90 mg of chloroprocaine injected into the subarachnoid space is unlikely to result in high or total spinal block.[1,2] From all indications, a 3-ml dose of 0.75 per cent *hyperbaric* bupivacaine (22.5 mg in 8.25 per cent or 8.0 per cent dextrose, specific gravity approximately 1.035) would do so.[3,4] However, 0.75 per cent bupivacaine used for epidural block is *isobaric* (specific gravity, 1.007) and up to 4 ml of a 0.5 per cent isobaric solution (20 mg, specific gravity 1.006) has been used safely for spinal anesthesia.[5,6] Morison and coworkers have injected 3 ml of a 0.75 per cent isobaric solution of bupivacaine unintentionally into the subarachnoid space while attempting intermittent epidural block in two parturients with no untoward sequelae, although analgesia to T1 and T4 ensued.[7] To date, we have not injected 3 ml of 0.75 per cent *isobaric* bupivacaine subarachnoidally, so that comments on its possible effects would only be conjecture. In summary, even if a test dose containing 22.5 mg of bupivacaine did result in high or total spinal anesthesia, it would be: 1) an expected possible result of a test dose; 2) in all probability immediately recognized; and 3) treated correctly, as in the previously noted cases.[7] Conversely, if a high or total spinal block occurs when not anticipated from a large dose—10 ml (75 mg) or more used to establish the required analgesia for an operative procedure—the outcome may be catastrophic. Furthermore, treating a high or total spinal block resulting from 22.5 mg, as compared to 75 mg or more, would seem to be a more desirable situation.

Secondly, Morison questions whether 3 ml of 1.5 per cent lidocaine or mepivacaine will produce significant spinal anesthesia in two minutes. A dose of 45 mg of either drug, whether it is in 3 ml (1.5 per cent solution) or in 0.9 ml (5 per cent solution) will consistently produce *clinical evidence* of spinal analgesia within two minutes (excluding technical errors). However, it may or may not produce analgesia adequate for a surgical procedure (*e.g.*, an intra-abdominal operation). Even reference 6 cited by Morison states that onset of anesthesia with lidocaine is almost immediate. Furthermore, a 2-ml ampule of 1.5 per cent lidocaine (30 mg) in 7.5 per cent dextrose is available for spinal anesthesia for vaginal deliveries, and it is effective.[8] Although mepivacaine is no longer available for spinal anesthesia, our experiences as well as a careful review of mepivacaine for spinal block support the effectiveness of 45 mg in producing *clinical evidence* of spinal anesthesia within two minutes.[9–14]

Finally, what really is needed is a single-dose ampule

that could be used as a test dose, regardless of what local anesthetic drug was chosen or whether the regional block was being used for a surgical, obstetrical, diagnostic, or therapeutic procedure. Such a single-dose ampule would hold 2 or perhaps 3 ml of solution containing: 1) 0.015 mg epinephrine to provide evidence of an intravascular injection; 2) 50 mg lidocaine which rapidly results in spinal block of short duration; and 3) 5.0 per cent to 7.5 per cent glucose as a vehicle to provide a specific gravity greater than cerebrospinal fluid, to eliminate the question as to whether the injected solution is iso-, hypo-, or hyperbaric. Although a 1-ml test dose might be more desirable, any loss of it prior to or during injection might result in equivocal results.

DANIEL C. MOORE, M.D.
MANBIR S. BATRA, M.D.
Staff Anesthesiologists
The Mason Clinic
Seattle, Washington 98111

REFERENCES

1. Foldes FF, McNall PG: 2-chloroprocaine: A new local anesthetic agent. ANESTHESIOLOGY 13:287–296, 1952
2. Nellermoe CW, Moore DC, Bridenbaugh LD, Casady GN, Braly B: A clinical appraisal of 2-chloroprocaine in continuous caudal obstetrical anesthesia. ANESTHESIOLOGY 21:269–272, 1960
3. Moore DC: Spinal anesthesia: Bupivacaine compared with tetracaine. Anesth Analg (Cleve) 59:743–750, 1980
4. Chambers WA, Littlewood DG, Edstrom HH, Scott DB: Spinal anaesthesia with hyperbaric bupivacaine: Effect of dose and volume administered. Br J Anaesth 54:75–80, 1982
5. Nolte H, Schikor K, Gregs P, Meyer J, Starr P: Zur frage der spinal anaesthesie mit isobaren bupivacaine 0.5%. Anaesthetist 26:33–37, 1977
6. Nightingale PJ, Martsand T: Subarachnoid anaesthesia with bupivacaine for orthopedic procedures in the elderly. Br J Anaesth 53:369–371, 1981
7. Fargas-Babjak A, McChesney J, Morison DH: The efficacy of bupivacaine 0.75 percent as an epidural test dose. Can Anaesth Soc J 27:500–501, 1980
8. Physicians' Desk Reference 35th ed. Oradell, Medical Economics Co, 1982, pp 610–611
9. Poe MF, Dornette WHL, Johnson CH: Clinical observations on the intrathecal use of mepivacaine. ANESTHESIOLOGY 23:678–681, 1962
10. Sadove MS, Sanchez JD: A clinical appraisal of mepivacaine hydrochloride (Carbocaine) in spinal anesthesia. J Int Coll Surg 39:45–54, 1963
11. Dunn RE, Gee HL, Carnes MA, Fabian LW: Spinal anesthesia with mepivacaine hydrochloride: A preliminary report. Anesth Analg (Cleve) 42:49–54, 1963
12. Siker ES, Wolfson B, Stewart WD, Pavilack P, Pappas MT: Mepivacaine for spinal anesthesia: Effects of changes in concentration and baricity. Anesth Analg (Cleve) 45:191–196, 1966
13. Lipton E, Sennott FW, Batt B: Mepivacaine for spinal anesthesia in vaginal delivery: An objective comparison with tetracaine. Am J Obstet Gynecol 96:333–336, 1966
14. Litarczek G, Fagarasonu R, Cristea I, Popescu D, Daruczi A: Clinical use of mepivacaine: Experience with 1248 cases. Anesth Analg (Cleve) 47:50–53, 1968

(Accepted for publication February 23, 1982.)

Anesthesiology
57:140–143, 1982

Relaxant Resistance in Disuse Atrophy: Pharmacokinetics *vs.* Pharmacodynamics

To the Editor:—With his recent article,[1] Dr. Gronert has stimulated our interest in muscle relaxant pharmacokinetics and dynamics in altered pathophysiologic states. In a canine model, he has observed an apparent resistance to pancuronium in immobilized, as opposed to active, extremities of the same animal. He concludes that there must be a pharmacodynamic reason for this difference in sensitivity. However, there is an alternative explanation for his results.

After bolus intravenous injection, the plasma concentration of a muscle relaxant will reach a peak immediately, and subsequently decline in a bi-exponential or tri-exponential fashion. However, the effect from that dose requires several minutes to reach a maximum, as we all know from clinical observation. Similarly, the decline in effect lags behind the decline in plasma concentration, and for moderate doses of relaxants, probably includes a component of redistribution as well as elimination of the drug.

Sheiner *et al.*[2] have described a kinetic model for this disequilibrium between plasma concentration and effect after a bolus dose. A rate constant, termed k_{eo}, can be calculated to quantify the time dependent lag between drug concentration in plasma and the site of action. Agents which affect muscle blood flow, such as halothane, have been shown to alter the $t_{1/2}$ k_{eo} for muscle relaxants.[3] If the equilibration time between plasma and the site of action is prolonged, as occurs with halothane, not only will the time to peak effect after a moderate bolus dose be longer, but the fractional effect remaining at a given time interval after the peak will be greater. Conversely, under conditions where muscle blood flow is increased, the peak effect may occur sooner and dissipate faster. It is evident that if one wishes to give repeated small doses of muscle relaxants and measure cumulative effect, the timing of both dosing and effect quantitation relative to this time lag will critically affect the apparent sensitivity to the drug. Sheiner *et al.*[2] demonstrate this relationship very clearly in a series of computer-simulated plasma concentration-response curves (fig. 7 of the article),[2] where a change in $t_{1/2}$ k_{eo}, the equilibration half-time, produces a parallel-shifted curve,