

## Clinical Reports

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### Epidural Anesthetic Dose Responses in Patients 20 to 80 Years Old

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Volumes of local anesthetic solution used for epidural anesthesia have ranged from 3 ml in elderly patients<sup>1</sup> to in excess of 40 ml in young individuals.<sup>2</sup> Smaller volumes are desirable as they cause less disturbance to circulation and respiration; however, larger volumes may be necessary for extensive operations. To provide safe satisfactory anesthesia for a variety of procedures, a knowledge of anesthetic effects obtained with a range of doses in each age group is needed.

Epidural dose requirements in patients have been reported for every decade of age expressed as a segmental dose requirement (SDR), that is, the number of milliliters of local anesthetic needed to anesthetize one spinal segment.<sup>1,3</sup> To calculate the volume to administer, one multiplies SDR by the number of segments to be anesthetized. Thus, a 60-year-old patient who had an SDR of 1 ml per spinal segment would be given 10 ml for ten segments and 20 ml for twenty segments. This approach assumes a linear dose response, but its validity has never been established.

To examine the validity of the segmental dose concept and to define anesthetic levels that develop after epidural injection of various doses of local anesthetic, 81 patients 20 to 80 years of age were studied. Twelve of these 81 patients had epidural anesthesia on two or more occasions, so that data from 103 anesthetic administrations were available. Results are presented according to three age groups to demonstrate changes in anesthetic dose response with age.

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#### METHODS

According to standard practice, each patient was interviewed preoperatively and received premedication according to age and physical status. Patients were excluded from the study when they had central nervous system disease, histories of lumbar disc operations or abnormalities of the vertebral column, abdominal distention due to intestinal obstruction, ascites or tumor, or a bleeding tendency, or were pregnant. The technique of administering epidural anesthesia was standardized, with the table horizontal throughout. Epidural puncture was performed with the patient in the lateral decubitus position via the midline approach at the L2-3 interspace, using an air-filled syringe for detection of loss of resistance. Injection of 0.75 per cent bupivacaine with freshly added 1:200,000 epinephrine was made at a rate of 1 ml/sec through a 17-gauge Tuohy needle. The total volume, which included a 2-ml test dose, varied according to the extent of operation planned. A catheter (Deseret 19-gauge Cat. no. 3904) was then inserted, fixed in place, and the patient turned to the supine position. Thirty minutes after injection, the number of dermatomes anesthetized was determined<sup>4</sup> by absence of pain in response to pinprick by counting upward from the fifth sacral segment. The relation between the number of spinal segments anesthetized and the dose injected was recorded for each group using linear regression analysis.

#### RESULTS

In patients 20 to 40 years of age there was a significant linear relationship between dose of local anesthetic administered and number of spinal segments anesthetized (fig. 1). To block ten segments these patients needed 12-13 ml bupivacaine, 0.75 per cent, and to anesthetize 20 segments, 25-27 ml were necessary. Only two of the 30 patients had values that differed appreciably from the regression line. On the other

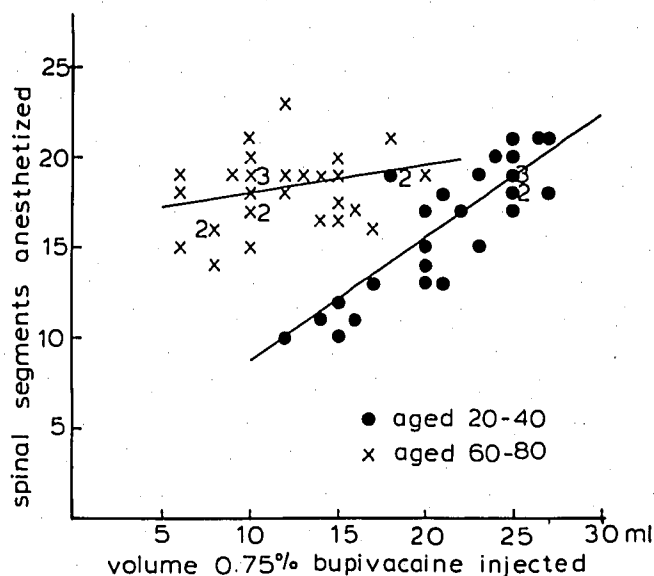


FIG. 1. Correlation between spinal segments anesthetized and volume of 0.75 per cent bupivacaine injected in patients aged 20 to 40 years ( $r = 0.827$ ,  $y = 0.681x + 1.907$ ,  $n = 28$ ,  $P < 0.0001$ ) and 60 to 80 years ( $r = 0.286$ ,  $y = 0.154x + 16.43$ ,  $n = 30$ , NS).

hand, mid- to upper-thoracic levels (T10–T1) developed in patients aged 60 to 80 years irrespective of the dose injected (fig. 1), and a direct dose response analogous to that in the younger patients was not seen. It was not possible to secure a low thoracic level reliably by injecting a smaller volume in these elderly patients, in whom volumes of 10 ml or less frequently resulted in anesthesia to the fourth thoracic dermatome or higher.

Results for patients aged 41 to 59 years are shown in figure 2. The regression line for patients aged 50 to 59 years lies somewhere between those shown for patients aged 20 to 40 years and patients aged 60 to 80 years. Results for patients 40 to 49 years old were not analyzed, but dose-response points were plotted individually and lay between the regression lines drawn for patients 20 to 40 years old and those 50 to 59 years old.

To examine further the dose responses in different age groups, 12 patients who had two operations were given different volumes of local anesthetic the second time. Anesthetic levels obtained are shown in figure 3. Most patients more than 50 years old experienced similar, if not identical, anesthetic levels with the two doses; that is, one 66-year-old patient was given 10 ml on one occasion and 20 ml on another, yet developed anesthesia of 19 segments both times. This is contrary to findings in a younger patient who had ten segments anesthetized with 15 ml, 15 segments with 20 ml, and 21 segments with 25 ml.

To examine the validity of the concept of SDR, values for SDR were calculated from data in figures 1 and 2, and plotted against volume injected (fig. 4). In

young patients the value for SDR did not vary with the volume injected, but averaged  $1.3 \pm 0.3$  ml per spinal segment. By contrast, patients aged 60 to 80 years showed no uniformity of results, but a range of values from 0.35 to 1.05 ml, depending on the volume injected. Values for SDR also varied with the volume injected, from 0.55 to 1.20 ml per segment, in patients aged 50 to 59 years. Therefore, predicting anesthetic levels using a single value for milliliters per spinal segment is invalid when the patient is more than 50 years of age, but applicable to patients aged 20 to 40 years.

#### DISCUSSION

The relationship between age and epidural dose requirements was examined by studying dose responses of patients aged 20 to 80 years. The decline in dose requirement with age has been verified, but the relationship is more complex than originally proposed.<sup>1</sup>

Patients 20 to 40 years old showed a direct relationship between dose injected and number of spinal segments anesthetized, enabling prediction of the number of segments anesthetized with a given dose of local anesthetic. However, this rule does not apply to patients more than 50 years old. Progressively more extensive anesthesia was obtained from a given dose of local anesthetic with advancing age, until, in patients more than 60 years old, mid- to upper-thoracic levels usually ensued irrespective of dose injected. Thus, it is difficult to limit the extent of anesthesia by injecting a smaller dose of anesthetic into an elderly patient.

The concept of SDR is invalid for patients more than

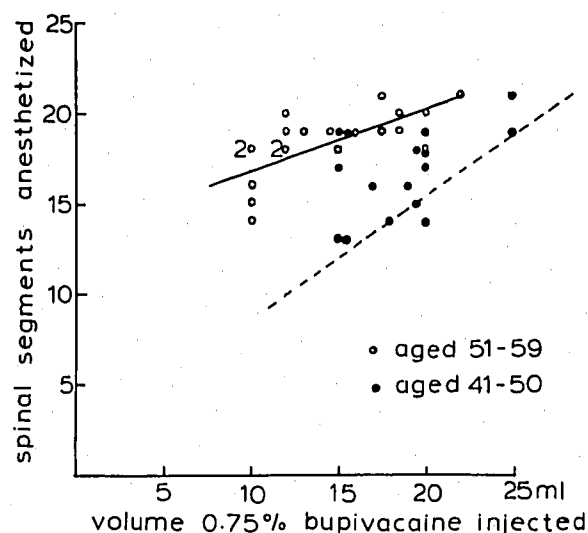


FIG. 2. Correlation between spinal segments anesthetized and volume of 0.75 per cent bupivacaine injected in patients aged 50 to 60 years (solid line) ( $r = 0.713$ ,  $y = 0.344x + 13.406$ ,  $n = 20$ ,  $P < 0.001$ ). Patients aged 40 to 49 years (closed circles) are plotted individually. The regression line for patients aged 20 to 40 years from figure 1 is drawn from comparison (interrupted line).

50 years old, for whom SDR is not unitary but a variable depending upon volume injected. The same conclusion may be reached by re-examining the data of Bromage.<sup>3,5</sup> Correlation coefficients between SDR and the volume of 2 per cent lidocaine injected were  $r = 0.89$ ,  $y = 0.029x + 0.264$  ( $P < 0.0001$ ) and  $r = 0.946$ ,  $y = 0.063x + 0.005$  ( $P < 0.0001$ ) in patients aged 60 to 80 and 80 to 100 years respectively. Linear regression equations had a similar slope in patients aged 60 to 80 years in the present study, suggesting that the variation of SDR with volume injected in older patients is not peculiar to bupivacaine, but may also be expected with other local anesthetics. It is suggested that, rather than calculate the volume of local anesthetic from a table of SDRs, one choose a unitary volume for a given age group. To obtain mid- to upper-thoracic dermatomal levels one may inject 20 to 25 ml into patients aged 20 to 40 years, 15 to 20 ml into patients aged 40 to 60 years, and as little as 6 to 10 ml into patients more than 60 years of age. More than 10 ml may be used in the elderly, but the reported cases of so-called "massive epidural" anesthesia in this age group have occurred when doses in excess of 15 ml have been used. These results apply only to the technique of epidural anesthesia chosen. Injections into the caudal, thoracic or even lower lumbar epidural space may have different dose requirements.<sup>6</sup> In addition, the concentration or type of local anesthetic used, the position of the patient during anesthesia, and the rate of injection may each influence the result.<sup>7</sup> In spite of utilization of a standardized technique, anesthetic levels obtained with a given volume of 0.75 per cent bupivacaine varied in each group of patients. This is probably due to hitherto unknown patient

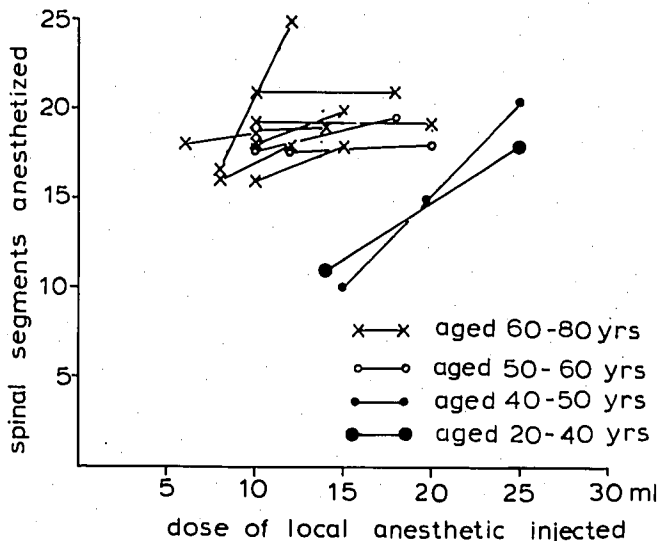


FIG. 3. Spinal segments anesthetized after injection of different doses of 0.75 per cent bupivacaine into the same patient on separate occasions.

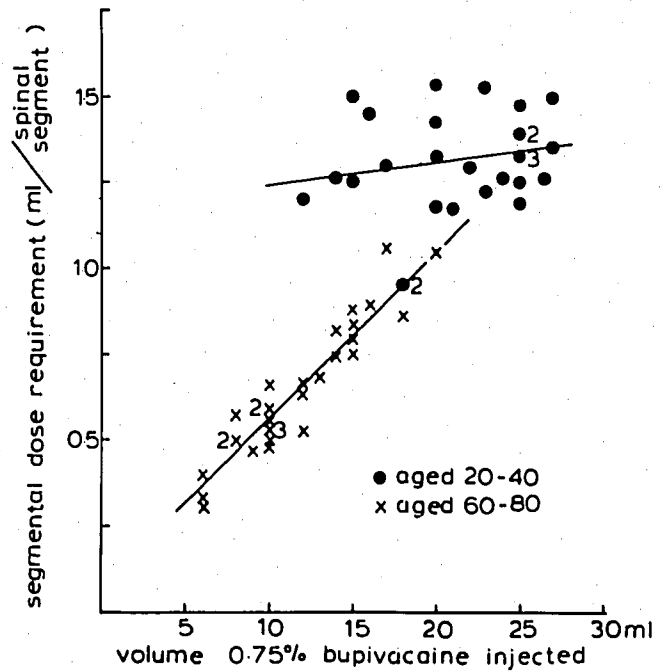


FIG. 4. Correlations between values for ml of bupivacaine per spinal segment (SDR) and volume injected for patients aged 20 to 40 years ( $r = 0.068$ ,  $y = 0.007x + 1.171$ ,  $n = 28$ , NS), 50 to 40 years, which are not plotted ( $r = 0.949$ ,  $y = 0.035x + 0.259$ ,  $n = 20$ ,  $P < 0.0001$ ) and 60 to 80 years ( $r = 0.944$ ,  $y = 0.049x + 0.059$ ,  $n = 30$ ,  $P < 0.0001$ ).

characteristics that influence spread of local anesthetic within the epidural space. Elucidation of these factors may make an epidural anesthesia a more precise form of anesthesia.

It is not easy to explain why the dose-response relation in the young differs from that in patients more than 50 years old. However, anatomic changes influence the pattern of spread of local anesthetic injected into the epidural space. Following lumbar epidural injection, radiopaque dye may be seen in the paravertebral spaces of young, but not elderly, patients.<sup>6</sup> Radioactivity after epidural injection of iodine-131 mixed in 2 per cent lidocaine is detectable more cephalad in patients more than 50 years old than in the young.<sup>8</sup> These findings suggest that with increasing age (probably about the fifth decade) the intervertebral foramina are progressively occluded, preventing egress of local anesthetic, thereby enabling a smaller volume to spread more extensively within the epidural space.

On the other hand, the predominant site of action of epidural anesthesia may change with age. The typical segmental blockade observed in the young may reflect a predominantly paravertebral site of action, whereas the widespread anesthesia with small volumes in the elderly could result from a more dominant action within the subarachnoid space. It has been suggested that, with age, the dura becomes more permeable to

local anesthetics owing to a progressive increase in size and number of arachnoid villi, providing a larger area through which local anesthetic can diffuse into the subarachnoid space.<sup>9</sup>

Only 29 sensory dermatomes can be anesthetized (excluding coccygeal and cranial nerves) by epidural anesthesia. Thus, a point at which an additional volume of local anesthetic ceases to provide further anesthesia must exist. In the elderly this may occur in the upper thoracic region, as doubling the volume in certain patients did not provide further anesthesia. Such a transition was not observed in this study in patients aged 20 to 40 years utilizing volumes of as much as 27 ml, but might have been observed if volumes approaching 40 ml had been injected.

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## Nitroprusside Toxicity in a Renal Transplant Patient

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In most previously reported cases of sodium nitroprusside (SNP) toxicity the patients have died.<sup>1-6</sup> There has been no report of SNP toxicity in a patient with a transplanted kidney, although these patients often need acute antihypertensive therapy.<sup>7,8</sup> We describe the occurrence of SNP toxicity in a patient with a single transplanted kidney who showed tachyphylaxis to the drug and needed large doses to control hypertension.

## REPORT OF A CASE

A 27-year-old 68-kg woman, who had received a cadaveric renal allograft two years previously, had had abdominal pain, nausea, vomiting, and fever for four days. Her immunosuppressive regimen included azothioprine, 150 mg, daily, and prednisone, 35 mg, on alternate days; renal hypertension was controlled with spironolactone, 150 mg, furosemide, 40 mg, hydralazine, 400 mg, propranolol, 120 mg, and methyldopa, 2,000 mg, daily. Four months previous to admission she had undergone exploratory laparotomy and repair of a hepatic laceration.

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The patient appeared acutely ill and was febrile (temperature 38.7 C orally). Heart rate was 88/min, blood pressure 160/120 torr, and respiratory rate 20/min. The abdomen was moderately distended, and there was acute tenderness and guarding in the right upper quadrant, where a 10-15 cm mass continuous with the lower edge of the liver was palpable. The remainder of the physical examination was unremarkable. Pertinent laboratory data included hematocrit 29 per cent, leukocyte count 28,800, with a shift to the left, serum creatinine, 141  $\mu$ mol/l (1.6 mg/100 ml), bilirubin 50  $\mu$ mol/l (2.8 mg/100 ml), lactate dehydrogenase 392 IU, serum glutamic oxaloacetic transaminase (SGOT) 24 IU, alkaline phosphatase 99 IU, amylase 127 U/100 ml; serum electrolytes were normal. Abdominal echography confirmed the presence of a 10-cm solid mass inferior to the right lobe of the liver. Exploratory laparotomy on that day revealed rupture of the gallbladder with a large intraperitoneal hematoma. Cholecystectomy was performed.

In the perioperative period, despite reinstatement of the preoperative antihypertensive therapy, hypertension became difficult to control, with arterial pressures as high as 200/120 torr. SNP was started at a dose of 4.0  $\mu$ g/kg/min, and control of hypertension was achieved only with progressive increases in the SNP dosage. Two days postoperatively, the requirement had reached 12.5  $\mu$ g/kg/min, a total of 1,120 mg of SNP in 48 hours with progressive oliguria (100 ml/8 h). After an hour at this high dose level, the level of consciousness became variable, ranging from hyperexcitability and combativeness to coma, without any localizing neurologic signs. Within another hour, her hemodynamic status was unstable, and she showed large fluctuations of blood pressure and heart rate. Blood-gas analysis at this time showed Pa<sub>o</sub>, 90 torr, Pa<sub>co</sub>, 30 torr, hydrogen ion concentration 63.1 nmol/l (pH 7.20), base excess -16 mmol/l. Electrolytes were normal. The patient