# The Epidural Test Dose: A Review

Joanne Guay, MD, FRCPC

Department of Anesthesia, Maisonneuve-Rosemont Hospital, University of Montreal, Canada

This review systematically examines the literature on the ability of the classical epidural test dose and other strategies to detect intravascular, intrathecal, or subdural epidural needle/catheter misplacement. For detection of simulated intravascular misplacements, a sensitivity (S) and a positive predictive value (PPV) ≥80 demonstrated by at least two randomized controlled trials coming from two different centers were determined for the following tests and patient populations: Nonpregnant adult patients = increase in systolic blood pressure (SBP) ≥15 mm Hg (S = 80–100 and 93–100; PPV = 80–100 and 83–100) or either an increase in SBP ≥15 mm Hg or an increase in heart rate ≥10 bpm after the injection of 10 (S = 100; PPV = 83–100) or 15 μg of epinephrine (S = 100; PPV = 83–100); pregnant patients = sedation, drowsiness, or dizziness within 5 min after the injection of 100 μg of fentanyl (S = 92–100; PPV = 91–95); and children = increase in SBP ≥15 mm Hg after the injection of 0.5 μg/kg of epinephrine (S = 81–100; PPV = 100). Conversely, more studies are required to determine the best strategies to detect intrathecal and subdural epidural needle/catheter misplacements in these three patient populations.

(Anesth Analg 2006;102:921–9)

The concept of first injecting a small dose of local anesthetic into the epidural space and then observing the patient for any signs of accidental intravascular or intrathecal injection was noted in the earliest texts on epidural anesthesia (1). Likewise, the term "test dose" was included in Dr Bromage's first textbook on epidural anesthesia (2). In 1981, Moore and Batra (3) proposed 45 mg of lidocaine with 15 μg of epinephrine as the ideal epidural test dose. The aim of an epidural test dose is to avoid the consequences of injecting a critical amount of local anesthetic or opioid either intravascularly, subdurally, or intrathecally. An ideal test dose should allow the detection of all needles/catheters misplaced in one of these three locations, should never gives a false-positive response that would lead to unnecessary catheter repositioning or manipulation, and should never induce serious side effects. The efficacy of the classic test dose in achieving this goal remains undetermined. Several case reports or case series have been published in which the test dose not only failed to identify the catheter misplacement but may even have induced a serious adverse event (4–6).

This review examines the ability of the classical test dose and other strategies to detect intravascular, intrathecal, or subdural epidural needle/catheter misplacement.

## Methods

The American National Library of Medicine's PUBMED was searched with the following keyword associations: "test dose AND epidural," "epidural AND ultrasound," "epidural AND noninvasive cardiac output monitoring," and "epidural AND Doppler." Reference lists of review articles obtained were checked for other possible relevant randomized controlled trials (RCT). For effectiveness (sensitivity [S] and positive predictive value [PPV]), only the highest level of evidence was kept: RCT > controlled clinical trial (CCT) > prospective cohort (observational) or case control study > retrospective study > case report. For RCTs and CCTs, the following data were extracted from texts or tables: number of patients included, number of tests administered, number of true- and false-positive tests, S, and PPV. Ss and PPVs obtained in experimental conditions (from the studies) were calculated when required. Each response to a definite dose of drug was considered as a separate test. For each test, data from a single study were pooled. When only one RCT or CCT was available, a 95% confidence interval (95% CI) for each S and PPV was calculated. Otherwise, Ss and PPVs are reported in percentages as range (from one study to another) for each test. From the known incidences of intravascular or intrathecal catheter misplacement in the clinical setup, and from the S and false-positive rates

Accepted for publication October 19, 2005.

Address correspondence and reprint requests to Dr. Joanne Guay, MD, FRCPC, Clinical Associate Professor, Anesthesia, Maisonneuve-Rosemont Hospital, 5415 L'Assomption Boulevard, Montreal, Quebec, Canada H1T 2M4. Address e-mail to joanne.guay@umontreal.ca.

DOI: 10.1213/01.ane.0000196687.88590.6b

©2006 by the International Anesthesia Research Society
0003-2999/06



© International Anesthesia Research Society. Unauthorized Use Prohibited.

obtained in experimental conditions, posttest probabilities (PTP) and cumulative PTPs (independent tests only) were also calculated and are provided in percentages. Data were analyzed using the JMP 5.01 software (SAS Institute Inc., Cary, NC) and GraphPad StatMate (GraphPad Software Inc., San Diego CA).

## Results

The incidence of unintended intravascular entry by epidural catheters is estimated to be between 4.9% and 7% in the obstetrical population (epidural catheter inserted in parturient women for analgesia or Cesarean delivery) (7–9) with less intravascular entry undetected by aspiration of 2.3% for single-orifice and 0.6% for multiorifice catheters (1:63,000 for top-up doses) (7,8,10,11). In children, the incidence of accidental intravascular entry by epidural needle/catheter may be as frequent as 5.6% (12), and aspiration alone without previous injection fails to detect up to 86% of vascular entries (12).

The best results for S from nonpregnant adults were achieved with observation of an increase in heart rate (HR) ≥10 bpm or an increase in systolic blood pressure (SBP) ≥15 mm Hg with 10 or 15 μg of epinephrine equal to a decrease in T wave amplitude ≥25% after the injection of 10 or 15 μg of epinephrine (S = 100) greater than a decrease in T wave amplitude ≥25% after the injection of 5 μg of epinephrine (S = 95–100) greater than an increase in SBP ≥ 15 mm Hg after the injection of 15 μg of epinephrine (S = 93–100) greater than an increase in HR ≥ 10 bpm after the injection of 22.5 μg of epinephrine equal to an increase in SBP ≥ 15 mm Hg after the injection of 22.5 μg of epinephrine (95% CI for S = 83–100) greater than an increase in SBP ≥ 15 mm Hg after the injection of 10 μg of epinephrine (S = 80–100). Of the above, a PPV of 100 could be achieved for a decrease in T wave amplitude ≥25% after the injection of 5, 10, or 15 μg of epinephrine. A PPV ≥80 was noted for an increase in SBP ≥15 mm Hg with epinephrine 10 or 15 μg and for an increase in HR ≥10 bpm or in SBP ≥15 mm Hg with 10 or 15 μg of epinephrine. A 95% CI ≥80 for PPV was found for an increase in HR ≥10 bpm and for an increase in SBP ≥15 mm Hg with the injection of 22.5 μg of epinephrine. Therefore, a combined S and PPV of 100 could be achieved only with the observation of a decrease in T wave amplitude ≥25% after the injection of 10 or 15 μg of epinephrine (Table 1).

Assuming an approximate rate of 3.3% of unrecognized accidental intravascular epidural catheter misplacement (28) using an increase in HR ≥10 bpm or in SBP ≥15 mm Hg with 10 or 15 μg of epinephrine would give a PTP of 14.6% for any of these two tests (10 or 15 μg of epinephrine).

The amplitude of an epinephrine response is attenuated by the following factors for HR: aging (18), previous administration of β-adrenergic blocking drugs (selective or nonselective) (15), the combination of midazolam (arousable by verbal command) and fentanyl (2 μg/kg IV) (29), isoflurane (hemodynamic responses to intravascular injection of test doses vary with dose of epinephrine and depth of anesthesia) (30), sevoflurane (2% end-tidal concentration) (20), spinal blockade (31) or high ($T_5$) thoracic epidural anesthesia combined with general anesthesia (32) but not by IV atropine (administered just before the test dose) (33), midazolam alone (29), oral clonidine (24), or low ($T_{10}$) thoracic epidural anesthesia (32). The increase in SBP is affected by isoflurane (30), spinal (31) or high thoracic ($T_5$) epidural anesthesia (32) but not by aging (18,34), β-adrenergic blocking drugs (15), the combination of midazolam and fentanyl (29), oral clonidine (24), sevoflurane (20), or low ($T_{10}$) thoracic epidural anesthesia (32). The T wave amplitude decrease is not affected by the combination of midazolam and fentanyl (29), sevoflurane anesthesia (21), or the electrocardiogram lead (I, II, III, or V (5)) monitored (35).

For pregnant women, the best results for S were achieved with fentanyl 100 μg (S = 92–100), Doppler precordium auscultation after the injection of 10 mL of agitated saline (95% CI for S = 89–100), an increase in HR >10 bpm after the injection of 10 or 15 μg of epinephrine (95% CI for S = 77 or 78–100), observation of both a metallic taste and tinnitus after the injection of 100 mg of lidocaine (95% CI for S = 79–100), and the injection of a combination of bupivacaine 12.5 mg + epinephrine 12.5 μg (95% CI for S = 75–100). Of the above, a PPV ≥80 was obtained for fentanyl 100 μg (PPV = 91–95), injection of 10 mL of agitated saline (95% CI for PPV = 89–100), and the combination of bupivacaine 12.5 mg + epinephrine 12.5 μg (95% CI for S = 82–100). Therefore, a combined S and PPV ≥80 could be achieved only for fentanyl 100 μg and the injection of 10 mL of agitated saline (Table 2).

Assuming a prevalence of vascular catheterization unidentified by aspiration alone of 2.3% for single-orifice catheters (7,8) and of 0.6% for multiorifice catheters (8,10), the PTP of epinephrine, fentanyl, and agitated saline, respectively, would be 8.0%, 21.3%, and 16% for single-orifice catheters and 2.2%, 6.5%, and 4.7% for multiorifice catheters. A positive response to 2 independent tests would give a PTP of 50% (epinephrine + fentanyl), 41.4% (epinephrine + agitated saline), and 68.7% (fentanyl + agitated saline) for single-orifice catheters and 20.5%, 15.3%, and 36% for multiorifice catheters, respectively, for the same combinations. A positive response to the three tests would give a PTP of 89% and 67.5% for single- and multiorifice catheters, respectively.

For children, best Ss were obtained with an increase in HR ≥10 bpm after the injection of 0.75 μg/kg of

© International Anesthesia Research Society. Unauthorized Use Prohibited.

**Table 1.** Identification of Intravascular Epidural Catheter Misplacement in Nonpregmant Adult Patients

| Intervention | Effectiveness | | | | | Harm potential |
|---|---|---|---|---|---|---|
| Epinephrine | ↑ Heart rate ≥ 10 bpm | ↑ Heart rate ≥ 20 bpm | ↑ Systolic blood pressure ≥ 15 mm Hg | ↑ Heart rate ≥ 10 bpm or ↑ systolic blood pressure ≥ 15 mm Hg | ↓ T wave amplitude ≥ 25% | |
| Epinephrine 5 μg | 2 RCT (13,14); S = 60–100; PPV = 100 | 1 RCT (15); S = 73 (95% CI = 52–88); PPV = 100 (95% CI = 82–100) | 3 RCT (13–15); S = 50–80; PPV = 90–100 | 1 RCT (14); S = 70 (95% CI = 46–88); PPV = 100 (95% CI = 77–100) | 2 RCT (13,14); S = 95–100; PPV = 100 | 3 RCT (13–15); no SAE; 95% CI = 0–5.4 |
| Epinephrine 7.5 μg | 1 RCT (16); S = 55 (95% CI = 32–77); PPV = 100 (95% CI = 72–100) | 1 RCT (16); S = 10 (95% CI = 1.2–32); PPV = 100 (95% CI = 16–100) | 1 RCT (16); S = 60 (95% CI = 36–81); PPV = 100 (95% CI = 74–100) | No data | No data | 1 RCT (16); no SAE, 95% CI = 0–17 |
| Epinephrine 10 μg | 3 RCT (13,14, 17); S = 70–100; PPV = 100 | 3 RCT (15,17, 18); S = 30–96; PPV = 100 | 5 RCT (13–15, 17,18); S = 80–100; PPV = 80–100 | 2 RCT (14,17); S = 100; PPV = 83–100 | 2 RCT (13,14); S = 100; PPV = 100 | 5 RCT (13–15,17,18); no SAE; 95% CI = 0–3.4 |
| Epinephrine 15 μg | 9 RCT (13,14, 16,17,19–23); S = 70–100; PPV = 100 | 10 RCT (15–20, 22–25); S = 20–100; PPV = 100 | 13 RCT (13–25); S = 93–100; PPV = 83–100 | 2 RCT (14,17); S = 100; PPV = 83–100 | 3 RCT (13,14, 21); S = 100; PPV = 100 | 13 RCT (13–25; no SAE; 95% CI = 0–1 |
| Epinephrine 22.5 μg | 1 RCT (16); S = 100 (95% CI = 83–100; PPV = 100 (95% CI = 83–100) | 1 RCT (16); S = 60 (95% CI = 36–81; PPV = 100 (95% CI = 74–100) | 1 (16) RCT; S = 100 (95% CI = 83–100; PPV = 100) (95% CI = 83–100) | No data | No data | 1 RCT (16); no SAE; 95% CI = 0–17 |
| Lidocaine | Any one of the following symptoms: feel different, tinnitus, strange sensation around the mouth, tingling in the fingers | | | | | |
| Lidocaine 0.5 mg/kg | 1 RCT (26); S = 50 (95% CI = 27–73); PPV = 100 (95% CI = 69–100) | | | | | No SAE; common clinical use |
| Lidocaine 1 mg/kg | 1 RCT (26); S = 95 (95% CI = 75–100); PPV = 100 (95% CI = 82–100) | | | | | No SAE; common clinical use |
| 2-Chloroprocaine | Any subjective symptoms compatible with local anesthetic toxicity | | | | | |
| 2-Chloroprocaine 60 mg | 1 RCT (27); S = 80 (95% CI = 44–98); PPV = 100 (95% CI = 63–100) | | | | | 1 RCT (27); no SAE; 95% CI = 0–37 |
| 2-Chloroprocaine 90 mg | 1 RCT (27); S = 87 (95% CI = 69–96); PPV = 100 (95% CI = 87–100) | | | | | 1 RCT (27); no SAE; 95% CI = 0–12 |
| Bupivacaine | | | | | | |
| Bupivacaine 25 mg | 1 RCT (27); S = 77 (95% CI = 58–90); PPV = 100 (95% CI = 85–100) | | | | | 1 RCT (27); no SAE; 95% CI = 0–12 |

RCT = randomized controlled trial; sensitivities (S) and positive predictive values (PPV) in range or 95% confidence intervals (95% CI) as well as absence of serious adverse avent (SAE) are given in percentages.

epinephrine (95% CI for S = 84–100), an increase in T wave amplitude ≥25% with 0.25 μg/kg of epinephrine (95% CI for S = 83–100), an increase in SBP ≥ 15 mm Hg with 0.5 μg/kg of epinephrine (S = 81–100), an increase in SBP ≥ 15 mm Hg with 0.75 μg/kg of epinephrine (95% CI for S = 70–99), an increase in HR ≥ 10 bpm after the injection of 0. 5 μg/kg of epinephrine (S = 67–100), or an increase in HR ≥10 bpm after the injection of 0.25 μg/kg of epinephrine (95% CI for S = 62–97). Of the above, a PPV of 100 was noted for an increase in SBP ≥15 mm Hg with 0.5 μg/kg of epinephrine and for an increase in HR ≥ 10 bpm after the injection of 0.5 μg/kg of epinephrine, and a 95% CI ≥ 80 for PPV was found for the other variables. Therefore, a combined S and PPV ≥80 was present for an increase in SBP ≥15 mm Hg with 0.5 μg/kg of epinephrine only. A combined 95% CI ≥ 80 for both S and PPV was achieved for an increase in HR ≥10 bpm after the injection of 0.75 μg/kg of epinephrine and for an increase in T wave amplitude ≥25% with 0.25 μg/kg of epinephrine (Table 3).

Assuming an incidence of catheter/needle epidural entry undetected by aspiration of 4.8% (12), the PTP of an increase in SBP ≥15 mm Hg after the injection of 0.5 μg/kg of epinephrine would be 67.1% (for this value, the 95% CI of the false-positive rate was used).

IV atropine improved the epinephrine response in children anesthetized with halothane (HR) (58) or sevoflurane (SBP) (55). IV (59) or oral clonidine did not modify a test based on SBP (57). Leads I, II, III, or V (5) of the electrocardiogram are equally effective for the detection of T wave amplitude changes under sevoflurane anesthesia (60).

Some studies on the use of isoproterenol (nonpregnant adults, pregnant women, and children) or ephedrine (pregnant women) as a test dose for epidural

© International Anesthesia Research Society. Unauthorized Use Prohibited.

**Table 2.** Identification of Intravascular Epidural Catheter Misplacement in Pregnant Women

| Intervention | Effectiveness | | | | Harm potential |
|---|---|---|---|---|---|
| Multiorifice catheter | 3 observational studies reported that the incidence of negative aspiration despite intravascular misplacement would be less than the one reported in a retrospective review study for single-orifice catheter (7,10,36,37). This would not apply to catheters that are partially withdrawn after a positive aspiration (36); PPV not studied | | | | No evident SAE |
| Reaspiration | 1 retrospective review indicates that blood aspiration may be initially negative and becomes positive immediately after the injection of local anesthetics (7); PPV not studied | | | | No evident SAE |
| Air | Doppler fetal heart rate monitor place over mother's precordium | | | | |
| 10 mL of agitated saline | 1 RCT (38); S = 100 (95% CI = 89–100; PPV = 100 (95% CI = 89–100) | | | | No evident SAE |
| Epinephrine | ↑ Heart rate ≥ 25 bpm | | ↑ Heart rate > 10 bpm | | |
| Epinephrine 5 μg | | | 1 CCT (39); S = 87 (95% CI = 60–98); PPV = 77 (95% CI = 50–93) | | |
| Epinephrine 10 μg | | | 1 CCT (39); S = 100 (95% CI = 77–100); PPV = 78 (95% CI = 52–94) | | |
| Epinephrine 15 μg | 1 RCT (40); S = 50 (95% CI = 19–81); PPV = 71 (95% CI = 29–96) | | 1 CCT (39); S = 100 (95% CI = 78–100); PPV = 79 (95% CI = 54–94) | | 2 RCT (39,40; no SAE but 8% incidence of transient abnormal fetal heart rate (95% CI = 1–26), 1 RCT showing a decrease of uteroplacental blood flow in women with abnormal placental blood flow resistance after epidural injection (41), 2 case reports with maternal supraventricular tachycardia after epidural injection in susceptible women (42,43), 2 animal studies confirming a decrease in uterine blood flow with IV epinephrine injection (44,45) |
| Lidocaine | Metallic taste | Tinnitus | Dizziness | Metallic taste + Tinnitus | |
| Lidocaine 100 mg | 1 RCT (46); S = 75 (95% CI = 48–93); PPV = 80 (95% CI = 52–96) | 1 RCT (46); S = 88 (95% CI = 62–99); PPV = 93 (95% CI = 68–100) | 1 RCT (46); S = 88 (95% CI = 62–99); PPV = 78 (95% CI = 52–94) | 1 RCT (46); S = 100 (95% CI = 79–100); PPV = 84 (95% CI = 60–97) | No SAE; common clinical use |
| 2-Chloroprocaine | | | | | |
| 2-Chloroprocaine 100 mg | 1 RCT (46); S = 44 (95% CI = 20–70); PPV = 70 (95% CI = 35–93) | 1 RCT (46); S = 56 (95% CI = 30–80); PPV = 90 (95% CI = 56–100) | 1 RCT (46); S = 88 (95% CI = 62–99); PPV = 78 (95% CI = 52–94) | 1 RCT (46); S = 81 (95% CI = 54–96); PPV = 81 (95% CI = 54–96) | 1 RCT (46); no SAE; 95% CI = 0–21 |
| Bupivacaine + epinephrine | No specific criteria mentioned but the investigator was blinded and had the following information: maternal heart rate, timing of uterine contractions, noninvasive arterial blood pressure measurements and subjective maternal symptoms of IV injection of the solution (palpitations, lightheadness and dizziness). | | | | |
| Bupivacaine 12.5 mg + epinephrine 12.5 μg | 1 RCT (47); S = 95 (95% CI = 75–100); PPV = 100 (95% CI = 81–100) | | | | 1 RCT (47); no SAE; 95% CI = 0–17 |
| Fentanyl | Sedation, drowsiness or dizziness within 5 min | | | | |
| Fentanyl 100 μg | 2 RCT (48, 49); S = 92–100; PPV = 91–95 | | | | 2 RCT (48,49); no SAE; 95% CI = 0–4, 1 case report of profound maternal respiratory depression 100 min after epidural injection (50). |

RCT = randomized controlled trial; CCT = controlled clinical trial (not randomized for that intervention); sensitivities (S) and positive predictive values (PPV) in range or 95% confidence intervals (95% CI) as well as absence of serious adverse event (SAE) are given in percentages.

© International Anesthesia Research Society. Unauthorized Use Prohibited.

**Table 3.** Identification of Intravascular Epidural Catheter Misplacement in Children

| Intervention | Effectiveness | | | | | | Harm potential |
|---|---|---|---|---|---|---|---|
| Reaspiration | 1 observational study indicates that blood aspiration may be initially negative and becomes positive immediately after the injection of local anesthetics (12); PPV not studied | | | | | | No evident SAE |
| Epinephrine | ↑ Heart rate ≥ 10 bpm | ↑ Heart rate ≥ 20 bpm | ↑ Systolic blood pressure ≥ 15 mm Hg | ↑ Systolic blood pressure ≥ 20% | ↑ T wave ≥ 25% | ↓ T wave ≥ 25% | |
| Epinephrine 0.125 μg/kg | 1 RCT (51); S = 35 (95% CI = 15–59); PPV = 100 (95% CI = 59–100) | No data | 1 RCT (51); S = 40 (95% CI = 19–64); PPV = 100 (95% CI = 63–100) | No data | 1 RCT (51); S = 65 (95% CI = 41–85); PPV = 75–100 | No data | 1 RCT (51); no SAE; 95% CI = 0–17 |
| Epinephrine 0.25 μg/kg | 1 RCT (51); S = 85 (95% CI = 62–97); PPV = 100 (95% CI = 81–100 | No data | 1 RCT (51); S = 60; (95% CI = 36–81); PPV = 100 (95% CI = 74–100) | No data | 1 RCT (51); S = 100; (95% CI = 83–100); PPV = 100 (95% CI = 83–100) | No data | 1 RCT (51); no SAE; 95% CI = 0–17 |
| Epinephrine 0.5 μg/kg | 7 RCT (51–57); S = 67–100; PPV = 100 | 3 RCT (54, 55,57); S = 48–80; PPV = 100 | 6 RCT (51,53–57); S = 81–100; PPV = 100 | 1 RCT (52); S = 67; (95% CI = 38–88); PPV = 100 (95% CI = 69–100) | 4 RCT (51,53, 54,57); S = 19–100; PPV = 67–100 | 1 RCT (54); S = 29 (95% CI = 11–52); PPV = 30 (95% CI = 12–54) | 7 RCT (51–57); no SAE; 95% CI = 0–2 |
| Epinephrine 0.75 μg/kg | 1 RCT (54); S = 100 (95% CI = 84–100); PPV = 100 (95% CI = 84–100) | 1 RCT (54); S = 57 (95% CI = 34–78; PPV = 100 (95% CI = 74–100) | 1 RCT (54); S = 91 (95% CI = 70–99); PPV = 100 (95% CI = 82–100) | No data | 1 RCT (54); S = 33 (95% CI = 15–57); PPV = 78 (95% CI = 40–97) | 1 RCT (54); S = 52; (95% CI = 30–74); PPV = 44 (95% CI = 24–65) | 1 RCT (54); no SAE; 95% CI = 0–16 |

RCT = randomized controlled trial; sensitivities (S) and positive predictive values (PPV) in range or 95% confidence intervals (95% CI) as well as absence of serious adverse event (SAE) are given in percentages.

catheter misplacement have been published. However, because the safety of injecting these substances in the epidural space has never been clearly established, these techniques will not be reported here.

In pregnant women, epidural catheter placement for labor analgesia or Cesarean delivery is associated with a 0.6%–1.6% frequency of dural puncture (8,61). However, a direct subarachnoid injection after a negative aspiration through the needle or the catheter is quite rare and has been estimated to be between 1 in 1750 (0.06%) and 1 in 126,000 (0.0008%) and can occur despite the use of a multiorifice catheter (10,61,62). In children, the incidence of accidental dural puncture associated with epidural techniques (caudal, lumbar, or thoracic) is reported to be 8 per 24,409 attempts (0.03%) (63).

No RCT demonstrating a combined S and PPV ≥80 were found for any of the substances evaluated to detect intrathecal catheter misplacement (lidocaine, bupivacaine, ropivacaine, or levobupivacaine). A CCT in pregnant women with 8 mg of bupivacaine achieved a combined 95% CI ≥ 80 for both S and PPV (83–100 for both values) (Table 4).

Even when assuming an approximate incidence as frequent as 0.6% of unintended subarachnoid block (28), the PTP is less than 6% for any of the following substances: lidocaine 45 mg and bupivacaine 15–20 mg (nonpregnant adult patients) or bupivacaine 8 mg (pregnant women).

There is actually no RCT or CCT evaluating the neurostimulation test (Tsui test) with one group of patients with a catheter within the intrathecal space and another with the catheter in the epidural space.

The incidence of catheter or needle subdural misplacement may be as frequent as 0.82% (69). It has clearly been demonstrated that a catheter cannot penetrate an intact dura mater (70). However, even when epidural blockade is performed by trained anesthesiologists, the needle may partly pierce the dura mater in up to 7% of the patients and create a potential passage for the catheter (71). A catheter may then enter the subdural space and either cannulate it or proceed through the subarachnoid membrane to penetrate the subarachnoid space (72). If the catheter is maintained within the subdural space, injection of the local anesthetic may produce a subdural block or tear the fragile subarachnoid membrane and produce a composite block or a spinal block. The latter could explain why it is possible to have a spinal block without any return of cerebrospinal fluid (CSF) through the catheter on first aspiration. For a subdural block, signs and symptoms will vary according to the catheter tip location. Because the subdural space has more capacity posteriorly and laterally where sensory fibers

© International Anesthesia Research Society. Unauthorized Use Prohibited.

**Table 4.** Identification of Intrathecal Epidural Catheter Misplacement in Adults

| Intervention | Effectiveness | Harm potential |
|---|---|---|
| Nonpregnant adult patients | | |
| Lidocaine | Inability to raise legs for more than 2 to 3 s at 4 min | |
| Lidocaine 45 mg | 1 CCT (64); S = 100 (95% CI = 78–100); PPV = 94 (95% CI = 70–99) | No SAE; common clinical use |
| Bupivacaine | Any sensation of warmth in the lower extremities at 3 min | |
| Bupivacaine 15–20 mg | 1 RCT (65); S = 82 (95% CI = 68–91); PPV = 100 (95% CI = 91–100) | 1 RCT (65); no SAE; 95% CI = 0–7 |
| Pregnant women | | |
| Reaspiration | In a small case series, reaspiration was positive in all patients when repeated after at least 3 mL of liquid (5)/PPV not studied | No evident SAE; common clinical use for saline without preservative |
| Bupivacaine | Total inability to raise a straight leg present in at least one leg at 10 min | |
| Bupivacaine 8 mg | 1 CCT (66); S = 100 (95% CI = 83–100); PPV = 100 (95% CI = 83–100) | 1 CCT (66); no SAE; 95% CI = 0–17, 1 case report of severe hypotension and respiratory distress requiring tracheal intubation when this dose was injected after catheter repositioning (67). |
| Ropivacaine | Bromage score ≥ 1 within 8 min | |
| Ropivacaine 15 mg | 1 RCT (68); S = 100 (95% CI = 74–100); PPV = 100 (95% CI = 74–100) | 1 RCT (68); no SAE; 95% CI = 0–27 |

RCT = randomized controlled trial; CCT = controlled clinical trial (not randomized for that intervention); sensitivities (S) and positive predictive values (PPV) in range or 95% confidence intervals (95% CI) as well as absence of serious adverse event (SAE) are given in percentages.

are located, a sensory block should be expected. However, a motor and sympathetic block will be present if the local anesthetic travels anteriorly. In Lubenow et al.'s (69) case series on 18 patients, symptoms were as follows: sensory levels much higher than expected from the dose of local anesthetic injected, no CSF aspirated, motor block in 10 of 18 patients, delayed onset more than 10 min in 11 patients (from 5 to 30 min), and hypotension ≥30% in 11 patients. Previous back surgery might be associated with an increase in the incidence of subdural block (69). The diagnosis can be confirmed by injecting a small volume of a contrast dye through the catheter and performing either a fluoroscopic or a computed tomography scan examination (73,74).

The classical test dose described by Moore and Batra (3)(lidocaine 45 mg with epinephrine 15 μg) may fail to reveal a subdural catheter misplacement (4). A recent case report described a woman in whom an intended epidural catheter was inadvertently placed 4 cm in the subdural space (needle at T10-11) without CSF return on catheter aspiration (diagnosis confirmed by computed tomography scan imaging) who had diffuse motor response (unilaterally at $T_3$ and bilaterally at $T_{10}$) with the neurostimulation test (0.8 mA) (74).

## Discussion

There are no absolute criteria to evaluate the effectiveness of a diagnostic test. However, in general, a test with a S less than 80 would not be considered effective. When the consequences of having a false-positive test are significant, a high PPV also seems advantageous. Moreover, before recommending the systematic use of a diagnostic test, other issues including: (a) reproducibility (from one center to another), (b) effectiveness (as judged by its S and PPV, for instance), (c) complexity and cost, (d) consequences of misdiagnosis, (e) possible side effects of the test inflicted on the patients who did not have the disease (or problem) and are submitted to it must be weighed. Finally, the quality of the studies evaluating the above issues must be considered.

Defining the effectiveness of the various strategies proposed as an epidural test dose with the following criteria: both a S ≥80 and a PPV ≥80 demonstrated by at least 2 RCT coming from 2 different centers, few strategies would meet these criteria. There is reasonable evidence for intravascular misplacement detection in nonpregnant adult patients (observation of an increase in SBP ≥15 mm Hg or either an increase in SBP ≥15 mm Hg or an increase in HR ≥10 bpm after the injection of 10 or 15 μg of epinephrine), intravascular misplacement detection in pregnant women (signs of sedation, drowsiness, or dizziness within 5 minutes after the injection of 100 μg of fentanyl), and intravascular misplacement detection in children (increase in SBP ≥15 mm Hg after the injection of 0.5 μg/kg of epinephrine) (Tables 1–4). Because the injection of these doses of epinephrine in these two subpopulations

© International Anesthesia Research Society. Unauthorized Use Prohibited.

(nonpregnant adult patients and children) have been extensively used without report of any serious side effects and the consequences of injecting large doses of local anesthetic intravascularly can be serious (75), a recommendation on their systematic use is reasonable.

When it comes to pregnant women however, the issue remains controversial. For the detection of intravascular catheter misplacement, the injection of epinephrine might be neither the best test (low PPV) nor have been sufficiently studied to be recommended, and significant side effects (decreased uteroplacental blood flow after IV or epidural injection) are possibly associated with its use (Table 2). Considering the infrequent incidence (0.6%) of undetected intravascular misplacement with the use of multiorifice catheters (8,10) and the small dose of local anesthetic administered to induce labor analgesia, some authors consider that the systematic injection of epinephrine in this situation is unjustified (36,37). They observe for failure to induce analgesia or sensory block after a small dose of local anesthetic, considering these cases possible undetected intravascular catheter misplacement. The risk benefit/ratio may differ when the epidural is performed for Cesarean delivery where the dose of local anesthetic is much larger and hence, consequences of a significant intravascular injection may be increased. Therefore, the routine addition of epinephrine in this situation may be reasonable and has been adopted by many anesthesiologists (76).

There is actually no RCT demonstrating that 45 mg of lidocaine would be more effective than any other strategy (including an alternate dose of lidocaine or injection of another local anesthetic) to detect intrathecal or subdural catheter misplacement or even demonstrating that lidocaine would be effective in detecting intrathecal or subdural catheter misplacement in any patient population. In addition, serious adverse events (total spinal block including respiratory paralysis, severe hypotension, and fetal bradycardia) have been associated with its use in pregnant women (5,6). Considering the extremely infrequent incidence of unrecognized intrathecal (0.53%) (28) or subdural (0.8%) (69) epidural catheter misplacement, a test with a PPV close to 100 in simulated situations is required to be clinically useful.

In conclusion, reasonable evidence can be found to recommend the systematic use of an epinephrine test dose in nonpregnant adult patients and in children for the detection of intravascular needle/catheter misplacement. For pregnant women, the epinephrine test dose might not be justified when a multiorifice catheter is inserted to induce labor analgesia. More studies are required to establish the best strategies to detect intrathecal and subdural catheter misplacement for all three patient populations.

## References

1. Dogliotti AM. A new method of block anesthesia: segmental peridural spinal anesthesia. Am J Surg 1933;20:107–18.
2. Bromage PR. Spinal epidural analgesia. Edinburgh and London: E & S Livingstone LTD, 1954:57–8.
3. Moore DC, Batra MS. The components of an effective test dose prior to epidural block. Anesthesiology 1981;55:693–6.
4. Crosby ET, Halpern S. Failure of a lidocaine test dose to identify subdural placement of an epidural catheter. Can J Anaesth 1989;36:445–7.
5. Richardson MG, Lee AC, Wissler RN. High spinal anesthesia after epidural test dose administration in five obstetric patients. Reg Anesth 1996;21:119–23.
6. Palkar NV, Boudreaux RC, Mankad AV. Accidental total spinal block: a complication of an epidural test dose. Can J Anaesth 1992;39:1058–60.
7. Kenepp NB, Gutsche BB. Inadvertent intravascular injections during lumbar epidural analgesia. Anesthesiology 1981;54: 172–3.
8. Pan PH, Bogard TD, Owen MD. Incidence and characteristics of failures in obstetric neuraxial analgesia and anesthesia: a retrospective analysis of 19,259 deliveries. Int J Obstet Anesth 2004; 13:227–33.
9. Leighton BL, Norris MC, DeSimone CA, et al. The air test as a clinically useful indicator of intravenously placed epidural catheters. Anesthesiology 1990;73:610–3.
10. Leighton BL, Topkis WG, Gross JB, et al. Multiport epidural catheters: does the air test work? Anesthesiology 2000;92: 1617–20.
11. Crawford JS. Epidural test dose in obstetrics. Can J Anaesth 1988;35:441–2.
12. Fisher QA, Shaffner DH, Yaster M. Detection of intravascular injection of regional anaesthetics in children. Can J Anaesth 1997;44:592–8.
13. Takahashi S, Tanaka M, Toyooka H. The efficacy of hemodynamic and T-wave criteria for detecting intravascular injection of epinephrine test dose in propofol-anesthetized adults. Anesth Analg 2002;94:717–22.
14. Tanaka M, Goyagi T, Kimura T, Nishikawa T. The efficacy of hemodynamic and T wave criteria for detecting intravascular injection of epinephrine test doses in anesthetized adults: a dose-response study. Anesth Analg 2000;91:1196–202.
15. Guinard JP, Mulroy MF, Carpenter RL, Knopes KD. Test doses: optimal epinephrine content with and without acute beta-adrenergic blockade. Anesthesiology 1990;73:386–92.
16. Tanaka M, Takahashi S, Kondo T, Matsumiya N. Efficacy of simulated epidural test doses in adult patients anesthetized with isoflurane: a dose-response study. Anesth Analg 1995;81: 987–92.
17. Schoenwald PK, Whalley DG, Schluchter MD, et al. The hemodynamic responses to an intravenous test dose in vascular surgical patients. Anesth Analg 1995;80:864–8.
18. Guinard JP, Mulroy MF, Carpenter RL. Aging reduces the reliability of epidural epinephrine test doses. Reg Anesth 1995;20: 193–8.
19. Takahashi S, Tanaka M, Toyooka H. Fentanyl pretreatment does not impair the reliability of an epinephrine-containing test dose during propofol-nitrous oxide anesthesia. Anesth Analg 1999; 89:743–7.
20. Takahashi S, Tanaka M. Reduced efficacy of simulated epidural test doses in sevoflurane-anesthetized adults. Can J Anaesth 1999;46:433–8.
21. Tanaka M, Nishikawa T. A comparative study of hemodynamic and T-wave criteria for detecting intravascular injection of the test dose (epinephrine) in sevoflurane-anesthetized adults. Anesth Analg 1999;89:32–6.
22. Tanaka M, Nishikawa T. Efficacy of simulated intravenous test dose in the elderly during general anesthesia. Reg Anesth Pain Med 1999;24:393–8.

© International Anesthesia Research Society. Unauthorized Use Prohibited.

23. Tanaka M, Nishikawa T. The combination of epinephrine and isoproterenol as a simulated epidural test dose in isoflurane-anesthetized adults. Anesth Analg 1998;86:1312–7.
24. Tanaka M, Nishikawa T. Oral clonidine premedication does not alter the efficacy of simulated intravenous test dose containing low dose epinephrine in awake volunteers. Anesthesiology 1997;87:285–8.
25. Tanaka M, Yamamoto S, Ashimura H, et al. Efficacy of an epidural test dose in adult patients anesthetized with isoflurane: lidocaine containing 15 micrograms epinephrine reliably increases arterial blood pressure, but not heart rate. Anesth Analg 1995;80:310–4.
26. Michels AM, Lyons G, Hopkins PM. Lignocaine test dose to detect intravenous injection. Anaesthesia 1995;50:211–3.
27. Mulroy MF, Neal JM, Mackey DC, Harrington BE. 2-Chloroprocaine and bupivacaine are unreliable indicators of intravascular injection in the premedicated patient. Reg Anesth Pain Med 1998;23:9–13.
28. Bonica JJ, Backup PH, Anderson CE, et al. Peridural block: an analysis of 3,637 cases and a review. Anesthesiology 1957;18: 723–37.
29. Tanaka M, Sato M, Kimura T, Nishikawa T. The efficacy of simulated intravascular test dose in sedated patients. Anesth Analg 2001;93:1612–7.
30. Liu SS, Carpenter RL. Hemodynamic responses to intravascular injection of epinephrine-containing epidural test doses in adults during general anesthesia. Anesthesiology 1996;84:81–7.
31. Liu SS, Stevens RA, Vasquez J, et al. The efficacy of epinephrine test doses during spinal anesthesia in volunteers: implications for combined spinal-epidural anesthesia. Anesth Analg 1997;84: 780–3.
32. Liu SS. Hemodynamic responses to an epinephrine test dose in adults during epidural or combined epidural-general anesthesia. Anesth Analg 1996;83:97–101.
33. Narchi P, Mazoit JX, Cohen S, Samii K. Heart rate response to an i.v. test dose of adrenaline and lignocaine with and without atropine pretreatment. Br J Anaesth 1991;66:583–6.
34. Tanaka M, Nishikawa T. Aging reduces the efficacy of the simulated epidural test dose in anesthetized adults. Anesth Analg 2000;91:657–61.
35. Tanaka M, Nishikawa T. Does the choice of electrocardiography lead affect the efficacy of the T-wave criterion for detecting intravascular injection of an epinephrine test dose? Anesth Analg 2002;95:1408–11.
36. Norris MC, Fogel ST, Dalman H, et al. Labor epidural analgesia without an intravascular 'test dose'. Anesthesiology 1998;88: 1495–501.
37. Norris MC, Ferrenbach D, Dalman H, et al. Does epinephrine improve the diagnostic accuracy of aspiration during labor epidural analgesia? Anesth Analg 1999;88:1073–6.
38. Leighton BL, Gross JB. Air: an effective indicator of intravenously located epidural catheters. Anesthesiology 1989;71: 848–51.
39. Colonna-Romano P, Lingaraju N, Godfrey SD, Braitman LE. Epidural test dose and intravascular injection in obstetrics: sensitivity, specificity, and lowest effective dose. Anesth Analg 1992;75:372–6.
40. Leighton BL, Norris MC, Sosis M, et al. Limitations of epinephrine as a marker of intravascular injection in labouring women. Anesthesiology 1987;66:688–91.
41. Marx GF, Elstein ID, Schuss M, et al. Effects of epidural block with lignocaine and lignocaine-adrenaline on umbilical artery velocity wave ratios. Br J Obstet Gynaecol 1990;97:517–20.
42. Stickles BJ. Idiosyncratic supraventricular tachycardia after epidural anesthesia. J Nurse Midwifery 1993;38:42–4.
43. Merson N. Adenosine treatment of supraventricular tachycardia following epidural test dose: a case study. AANA J 1993;61: 521–3.
44. Chesnut DH, Weiner CP, Herring JE, Wang J. Effect of intravenous epinephrine upon uterine blood flow velocity in the pregnant guinea pig. Anesthesiology 1986;65:633–6.
45. Hood DD, Dewan DM, James FM. Maternal and fetal effects of epinephrine in gravid ewes. Anesthesiology 1986;64:610–3.
46. Colonna-Romano P, Lingaraju N, Braitman LE. Epidural test dose: lidocaine 100 mg, not chloroprocaine, is a symptomatic marker of i.v. injection in labouring parturients. Can J Anaesth 1993;40:714–7.
47. Gieraerts R, Van Zundert A, De Wolf A, Vaes L. Ten mL bupivacaine 0.125% with 12.5 micrograms epinephrine is a reliable epidural test dose to detect inadvertent intravascular injection in obstetric patients: a double-blind study. Acta Anaesthesiol Scand 1992;36:656–9.
48. Yoshii WY, Miller M, Rottman RL, et al. Fentanyl for epidural intravascular test dose in obstetrics. Reg Anesth 1993;18:296–9.
49. Morris GF, Gore-Hickman W, Lang SA, Yip RW. Can parturients distinguish between intravenous and epidural fentanyl? Can J Anaesth 1994;41:667–72.
50. Brockway MS, Noble DW, Sharwood-Smith GH, McClure JH. Profound respiratory depression after extradural fentanyl. Br J Anaesth 1990;64:243–5.
51. Tanaka M, Nishikawa T. The efficacy of a simulated intravascular test dose in sevoflurane-anesthetized children: a dose-response study. Anesth Analg 1999;89:632–7.
52. Tyagi A, Sethi AK, Chatterji C. Comparison of isoprenaline with adrenaline as components of epidural test dose solutions for halothane anaesthetized children. Anaesth Intensive Care 2002; 30:29–35.
53. Kozek-Langenecker SA, Marhofer P, Jonas K, et al. Cardiovascular criteria for epidural test dosing in sevoflurane- and halothane-anesthetized children. Anesth Analg 2000;90:579–83.
54. Sethna NF, Sullivan L, Retik A, et al. Efficacy of simulated epinephrine-containing epidural test dose after intravenous atropine during isoflurane anesthesia in children. Reg Anesth Pain Med 2000;25:566–72.
55. Tanaka M, Nishikawa T. Simulation of an epidural test dose with intravenous epinephrine in sevoflurane-anesthetized children. Anesth Analg 1998;86:952–7.
56. Tanaka M, Nishikawa T. Evaluating T-wave amplitude as a guide for detecting intravascular injection of a test dose in anesthetized children. Anesth Analg 1999;88:754–8.
57. Shiga M, Nishina K, Mikawa K, et al. Oral clonidine premedication does not change efficacy of simulated epidural test dose in sevoflurane-anesthetized children. Anesthesiology 2000;93: 954–8.
58. Desparmet J, Mateo J, Ecoffey C, Mazoit X. Efficacy of an epidural test dose in children anesthetized with halothane. Anesthesiology 1990;72:249–51.
59. Burstal R, Hollard J, McFadyen B. Simulated epidural test doses using adrenaline and adrenaline/clonidine in sevoflurane-anaesthetized children. Anaesth Intensive Care 2003;31:362–70.
60. Ogasawara K, Tanaka M, Nishikawa T. Choice of electrocardiography lead does not affect the usefulness of the T-wave criterion for detecting intravascular injection of an epinephrine test dose in anesthetized children. Anesth Analg 2003;97:372–6.
61. Okell RW, Sprigge JS. Unintentional dural puncture: a survey of recognition and management. Anaesthesia 1987;42:1110–3.
62. Reynolds F, Speedy HM. The subdural space: the third place to go astray. Anaesthesia 1990;45:120–3.
63. Giaufre E, Dalens B, Gombert A. Epidemiology and morbidity of regional anesthesia in children: a one-year prospective survey of the French-Language Society of Pediatric Anesthesiologists. Anesth Analg 1996;83:904–12.
64. Colonna-Romano P, Padolina R, Lingaraju N, Braitman LE. Diagnostic accuracy of an intrathecal test dose in epidural analgesia. Can J Anaesth 1994;41:572–4.
65. Kalso E, Aromaa U, Tammisto T. Sensitivity, specificity and predictive value of the sensation of warmth as a method of detecting inadvertent subarachnoid injection of local anaesthetic when performing extradural blocks. Br J Anaesth 1991; 66:614–6.
66. Prince GD, Shetty GR, Miles M. Safety and efficacy of a low volume extradural test dose of bupivacaine in labour. Br J Anaesth 1989;62:503–8.

© International Anesthesia Research Society. Unauthorized Use Prohibited.

67. Stone PA, Thorburn J, Lamb KS. Complications of spinal anaesthesia following extradural block for caesarean section. Br J Anaesth 1989;62:335–7.
68. Ngan Kee WD, Khaw KS, Lee BB, et al. The limitations of ropivacaine with epinephrine as an epidural test dose in parturients. Anesth Analg 2001;92:1529–31.
69. Lubenow T, Keh-Wong E, Kristof K, et al. Inadvertent subdural injection: a complication of an epidural block. Anesth Analg 1988;67:175–9.
70. Hardy PAJ. Can epidural catheters penetrate dura mater: an anatomical study. Anaesthesia 1986;41:1146–7.
71. Metha M, Salmon N. Extradural block: confirmation of the injection site by x-ray monitoring. Anaesthesia 1985;40: 1009–12.
72. Blomberg RG. The lumbar subdural extraarachnoid space of humans: an anatomical study using spinaloscopy in autopsy cases. Anesth Analg 1987;66:177–80.
73. Wills JH. Rapid onset of massive subdural anesthesia. Reg Anesth Pain Med 2005;30:299–302.
74. Lena P, Martin R. Subdural placement of an epidural catheter detected by nerve stimulation. Can J Anaesth 2005;52:618–21.
75. Albright GA. Cardiac arrest following regional anesthesia with etidocaine or bupivacaine. Anesthesiology 1979;51:285–7.
76. Hughes SC, Levinson G, Rosen MA. Anesthesia for caesarean section. In: Hughes SC, Levinson G, Rosen MA, eds. Shnider and Levinson's anesthesia for obstetrics. 4th ed. Philadelphia: Lippincott Williams & Wilkins, 2002:201–36.

© International Anesthesia Research Society. Unauthorized Use Prohibited.