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Update on Modalities and Techniques for Labor Epidural Analgesia and Anesthesia

Anthony Chau, MD, FRCPC, MMSc[a,b,*], Lawrence C. Tsen, MD[c]

[a]Department of Anesthesia, B.C. Women's Hospital, 4500 Oak Street, Vancouver, BC V6H 3N1, Canada; [b]Department of Anesthesiology, Pharmacology and Therapeutics, Diamond Health Care Centre, 11th Floor, 2775 Laurel Street, Vancouver, BC V5Z 1M9, Canada; [c]Department of Anesthesiology, Perioperative and Pain Medicine, Brigham and Women's Hospital, 75 Francis Street, Boston, MA 02115, USA

Keywords

• Labor analgesia • Epidural analgesia • Dural puncture epidural
• Combined spinal epidural • Obstetric anesthesia • Continuous epidural infusion
• Programmed intermittent epidural bolus • Maintenance of labor analgesia

Key points

- Labor epidural analgesia and anesthesia initiation and maintenance techniques have evolved in an effort to enhance patient safety, outcomes and satisfaction.
- The dural puncture epidural technique has gained increasing research attention and popularity owing to evidence showing improved block quality and side effect profiles.
- Many centers have adopted the programmed intermittent epidural bolus regimen for epidural maintenance, given the multiple benefits observed over the continuous epidural infusion regimen.

INTRODUCTION

Neuraxial labor analgesia is the foundation of contemporary obstetric anesthesia practice. Continuous epidural technique (EPL) and combined spinal epidural (CSE) technique are currently the most established and widely

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*Corresponding author. Department of Anesthesia, B.C. Women's Hospital, 4500 Oak Street, Vancouver, BC V6H 3N1, Canada. *E-mail address:* Anton.chau@ubc.ca

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practiced methods for initiating labor epidural analgesia. Recently, the dural puncture epidural (DPE) technique has gained increasing research attention and popularity owing to evidence showing improved block characteristics and side effect profiles in the obstetric population [1–3].

As techniques for initiation of neuraxial analgesia were undergoing refinement, methods for maintenance of intrapartum neuraxial analgesia were also evolving. In the past, epidural analgesia following the initial loading dose was maintained by manual boluses of concentrated local anesthetic solutions by the provider. With the advent of electronic pumps, the combination of continuous epidural infusions (CEI) and patient-controlled epidural analgesia (PCEA) became the standard method of labor analgesia maintenance. The desire to further improve labor analgesia and minimize side effects has led to the use of more dilute local anesthetic solutions and the programmed intermittent epidural bolus (PIEB) maintenance regimen.

This article provides an overview of the history, and compares and contrasts various neuraxial techniques that are currently used to initiate and maintain labor epidural analgesia, with an emphasis on novel techniques. The advantages and disadvantages of each technique in different clinical contexts are discussed. In addition, current gaps in evidence are outlined and future investigations are suggested to help advance knowledge in this area.

HISTORY OF NEURAXIAL LABOR ANALGESIA

In 1847, at a time when many thought that "God had ordained that women should suffer during childbirth", Scottish obstetrician James Young Simpson marked an important moment in the history of obstetric anesthesia when he introduced the use of diethyl ether to facilitate a difficult vaginal delivery [4]. Almost half a century later, German surgeon August Bier successfully performed the first "cocainization of the spinal cord" in a patient undergoing ankle surgery, and this was promptly followed by successful reports of spinal anesthesia blockade in 167 patients by French surgeon Theodore Tuffier [5]. Impressed by these accounts and experiences, Swiss obstetrician Oscar Kreis introduced the "medullary narcosis technique" using intrathecal cocaine for labor analgesia in 6 parturients [6]; shortly after, in 1902, S.R. Hopkins published the superiority of spinal anesthesia for cesarean delivery compared with ether or chloroform in the *Journal of American Medical Association*. Although many more successful cases soon followed, reports of complications (eg, high blocks, neurologic injuries, and death) also started to emerge [7]. These reports were rare and improved the understanding of potential spinal anesthetic-related complications among the anesthesia providers, but neuraxial analgesia and anesthesia were also condemned by some obstetric authorities and consequently their use had declined for a short period of time [8]. It was not until 1931, when Romanian obstetrician Eugen Aburel presented his technique of continuous epidural block for labor analgesia at a meeting in Paris, that neuraxial techniques were once again reinvigorated in obstetrics. Subsequently, several important events took place between the 1930s and 1980s, such as the development of the loss-of-resistance technique, report of the first CSE technique, invention of the Tuohy needle, and description of the use of epidural morphine. By the 1980s, neuraxial labor epidural analgesia became widely available and pain relief became an expectation of many parturients [9]. In 1996, Suzuki and colleagues [10] published the first study on the DPE technique in patients undergoing lower abdominal surgery. Around the same time, Kodali [11] first reported improved spread and block quality using intermittent epidural boluses. The findings from these reports marked the beginning of a series of investigations on the DPE and PIEB techniques. In the last decade, Tsen and colleagues have accumulated more evidence on the effect of the DPE technique on maternal and fetal outcomes, whereas numerous studies have established a clear advantage of PIEB compared with CEI, leading to more centers adopting the PIEB technique for maintenance of labor analgesia (Table 1).

Table 1
Chronology of selected events in the evolution of neuraxial analgesia and anesthesia for labor and delivery

1885	Leonard James Corning	Described spinal anesthesia while experimenting with cocaine in dogs
1890	Walter Wynter and Heinrich Quincke	Described and performed dural puncture
1898	August Bier	First public demonstration of successful spinal anesthesia for leg and pelvic operations; reported the first PDPH
1900	Oscar Kreis	Used spinal cocaine in 6 parturients
1921	Fidel Pagés Miravé	Described lumbar epidural anesthesia technique
1931	Eugen Bogdan Aburel	Instituted continuous caudal block with soft catheter
1932	Alberto Gutierrez and Achille Mario Dogliotti	Independently developed the loss of resistance and hanging drop technique to identify the epidural space
1937	Angelo Luigi Soresi	First to describe CSE anesthesia technique
1944	Edward Tuohy	Invented the Tuohy needle
1949	Charles E. Flowers	Reported the use of continuous epidural analgesia for labor, vaginal deliveries and operative deliveries
1949	J.G. Cleland	Described epidural analgesia using a Tuohy needle and epidural catheter
1979	M. Behar et al	Published the first report on epidural morphine for pain
1988	Gambling et al	Published the first study on PCEA for labor pain
1993	B.M. Morgan	Reported CSE technique for labor analgesia using needle-through-needle technique
1996	Nobuaki Suzuki et al	Published the first study on the DPE technique
1999	A.M. Kaynar and Bhavani S. Kodali	First to describe intermittent bolus of epidural catheter resulting in wider spread and better block quality than continuous infusion
2004	Sebastian M.H. Chua and Alex T.H. Sia	Published the first study on automated intermitted epidural boluses in labor analgesia
2005	Thomas et al	Published the first study using the DPE technique in the obstetric population
2008	Lawrence C. Tsen	Popularized use of dural puncture epidural in labor analgesia and coined the acronym DPE

Abbreviation: PDPH, post–dural puncture headache.

TECHNIQUES FOR INITIATION OF NEURAXIAL LABOR ANALGESIA

Epidural technique

The EPL has a long history of safety and efficacy in obstetric patients. With a syringe attached to an epidural needle, the loss of resistance to saline or air is used to locate the epidural space; subsequent passage of a catheter into the epidural space through the epidural needle allows administration of local anesthetic solutions that provide continuous, titratable labor analgesia or surgical anesthesia for cesarean delivery or other operative procedures.

The EPL provides a more gradual onset of blockade, especially for the initial placement in which there are no prior medications within the epidural space. The slower onset (compared with spinal anesthesia), coupled with the ability to titrate the dermatomal level of the block, is advantageous in situations in which the potential for rapid onset of sympathetic blockade (and associated large hemodynamic swings) would be detrimental, as in parturients with cardiac or respiratory comorbidities. In a retrospective cohort analysis of 107 pregnancies in 65 women with moderate to complex congenital heart disease or pulmonary hypertension over a 12-year period, the EPL was found to be the most commonly used technique, compared with CSE, single-shot spinal, or general anesthesia [12].

Correct anatomic placement of an epidural catheter can be challenging and requires multiple attempts in some cases, particularly when performed by a novice provider, or in patients with high body mass index or scoliosis. Studies have reported that approximately 20 to 25 procedures are required before improvement in EPL is shown by anesthesia trainees [13], and a mean of approximately 50 attempts to reach competence [14]. Lumbar ultrasonography has been shown to improve the learning curve and can facilitate placement by more accurately locating midline, finding the depth of the ligamentum flavum, and identifying other surrounding structures [15].

Spinal technique

Single-shot spinal

The single-shot spinal technique is a reliable method of analgesia and anesthesia with a clear, visible end point of success (ie, cerebrospinal fluid [CSF] return) and rapid onset of action. This technique involves passing a spinal needle past the dura-arachnoid membrane, observing for CSF return, and subsequently administering medications consisting of a local anesthetic agent with or without opioids. Most commonly, 25-gauge to 27-gauge pencil-point spinal needles are used; the smaller caliber needles are associated with a lower risk of post–dural puncture headache (PDPH).

The single-shot spinal technique has the most rapid onset because medications are injected into the CSF, directly bathing the spinal cord and nerve roots; this bypasses the diffusion through the dura needed with epidural administration. The choice and baricity (density of local anesthetic relative to CSF) of the intrathecal local anesthetic can further affect its speed of onset. A recent review found that hyperbaric compared with isobaric bupivacaine administered at the lumbar (L4–5) spinal level had more rapid onset of sensory blockade to the fourth thoracic vertebra (T4) level [16]. Given its quick speed of onset, the single-shot spinal technique is particularly useful for time-critical situations such as urgent or emergent operative deliveries.

This technique can also be used immediately before precipitous labor and vaginal delivery, instrumented delivery (eg, vacuum or forceps), expected episiotomy, or postpartum repair of perineal tears or lacerations. The type and dose of spinal anesthetic in these scenarios depend on the communication between the obstetrician and anesthesiologist; the onset and duration of the selected agent should consider the optimal setting for administration (eg, whether an instrumented or operative delivery is expected, consideration for additional space, personnel and resources needed, whether procedure would benefit from being performed in the operating room).

Continuous spinal

The continuous spinal technique is a useful and reliable method of analgesia and anesthesia in obstetric patients. Most often, insertion of a spinal catheter is done following an inadvertent dural puncture during an attempted epidural placement. However, intentional continuous spinal technique has been used to achieve successful, titratable, rapid-onset surgical anesthesia for parturients with high-risk cardiac conditions [17,18] and morbid obesity [19]. Patients with restricted local anesthetic spread in the epidural space caused by scarring from prior surgery, and who require a titratable method of reliable analgesia and anesthesia, may also benefit from this technique.

Clinically, a high incidence of PDPH [20], neurologic complications [21], dosing error caused by a spinal catheter being mistaken for epidural catheter [22], and technical difficulties [23–25] (difficulty threading the catheter, difficulty removing the catheter, kinking of the catheter leading to failure, and catheter displacements) have limited the routine use of continuous spinal analgesia. Furthermore, rare cases of CSF-cutaneous fistula have been observed [26]. In the 1980s, microcatheters ($\leq$24 gauge) were successfully used to provide titratable segmental blockade; however, neurologic complications following the use of high-concentration, hyperbaric local anesthetic solutions led to their ban in the United States in 1992 [27]. Although such microcatheters continue to be used successfully in Europe, the continuous spinal technique in North America typically requires standard epidural catheters placed through 17-gauge or 18-gauge epidural needles. Newer intrathecal catheter systems, including a flexible 23-gauge catheter over a 27-gauge pencil-point spinal needle [28], have been introduced and further investigation into their efficacy and safety, including appropriate local anesthetic selection and dosing parameters, will be needed.

There is considerable debate on the best course of action following an inadvertent dural puncture during an epidural placement. In this scenario, anesthesia providers may choose to either insert an intrathecal catheter and convert to a continuous spinal analgesia technique or to remove the epidural needle and reattempt insertion at another level. Retrospective studies have found that placement of an intrathecal catheter may reduce the risk of another dural puncture, PDPH, and epidural blood patch rates [29], although a prospective, multicenter, controlled study did not support this hypothesis [30]. Moreover, even continuous spinal techniques can provide insufficient analgesia and/or anesthesia, particularly over time, and may need to be replaced by another neuraxial technique or converted to an alternative form of analgesia/anesthesia [31]. If repeating the EPL at an alternative level is chosen, the provider should be aware of the possibility of increased medication spread (eg, similar to a DPE technique; discussed later) or inadvertent threading of the catheter into the spinal space via the dural puncture.

Combined spinal epidural technique

Standard combined spinal epidural technique

Although the use of EPL became more widespread, many providers recognized the limitations inherent in the slower onset of sensory blockade and increased frequency of dense motor blockade, even when dilute concentrations of bupivacaine 0.0625% and 0.125% were used. Subsequently, Collis and colleagues [32] described a CSE technique that used a subarachnoid injection of bupivacaine 2.5 mg and fentanyl 25 μg, to achieve rapid analgesia (ie, within 3 minutes) with limited motor block (ie, observed in 3% of patients) [32].

In a standard CSE technique, a spinal needle (commonly 25–27 gauge) is passed through the epidural needle to puncture the dura-arachnoid membrane and enter the subarachnoid space. With visualization of CSF return at the hub of the spinal needle, a local anesthetic agent, opioid, or both are administered. A catheter is then inserted through the epidural needle into the epidural space to provide ongoing analgesia.

Two technical modifications to the CSE technique have emerged: (1) the sequential CSE technique and (2) epidural volume extension (EVE). Although these techniques have been investigated to improve labor analgesia [33], both are more commonly used for conversion of labor analgesia to cesarean delivery anesthesia.

Sequential combined spinal epidural technique

In sequential CSE, a smaller spinal dose of local anesthetic with or without opioid is administered directly into the spinal space, followed by initiation of a continuous epidural administration of local anesthetic agents. This technique requires more time to achieve the desired sensory blockade and is usually chosen to avoid the rapid sympathetic blockade from a typical (and larger) dose used with single-injection spinal anesthesia techniques. Unlike a de novo EPL, the sequential CSE technique harnesses the spinal space so that the lower lumbosacral nerves can be blocked densely and reliably by the intrathecal component, whereas the higher thoracolumbar nerves can be blocked by slowly titrating the epidural component. In healthy parturients undergoing elective cesarean delivery, there is no benefit in terms of cardiovascular stability of sequential CSE to standard CSE [34]. However, in parturients with comorbid conditions, such as uncorrected valvular lesions, myasthenia gravis, or short stature, a slower increasing sensory block via sequential CSE technique has been argued to enhance patient safety by offering greater hemodynamic control. As such, multiple case reports of parturients with various cardiopulmonary and genetic conditions have advocated the use of a sequential CSE rather than standard CSE to minimize hemodynamic fluctuations during cesarean delivery [35–41].

Epidural volume expansion

In the EVE technique, a reduced dose of local anesthetic is initially administered into the spinal space to achieve a sensory blockade; subsequently, the blockade is extended cephalad by the administration of volume (either in the form of local anesthetic or saline) into the epidural space via the epidural catheter [42]. The term EVE has evolved over time to be associated most commonly with the injection of saline rather than local anesthetic [43]. Multiple studies in pregnant [44,45] and nonpregnant [46–50] patients have shown that volume expansion with the use of epidural solution (5–10 mL) can result in median dermatomal increase of 1 to 4 levels. Although the optimal epidural volume for EVE has not been established, some clinicians suggest there may be a ceiling effect to block extension. Doganci and colleagues [51] randomized nonpregnant patients undergoing elective lower limb surgery to receive 0, 5, 10, 15, or 20 mL of saline using the EVE technique following a standardized dose of spinal anesthetic and found that the duration of analgesia and time to regression to L1 was longest in patients receiving saline 15 mL.

Although further investigation is warranted, the use of the EVE technique during cesarean delivery has become less popular because of reports of failed extension or inadequate density of blockade. Similarly, the use of the EVE technique did not offer superior labor analgesia compared with a standard CSE technique [33].

Dural puncture epidural technique

The DPE technique is the latest development in the evolution of labor neuraxial techniques. Similar to the CSE technique, the DPE technique involves first locating the epidural space with the epidural needle and then passing a spinal needle through the shaft of the epidural needle to create a dural puncture with CSF confirmation; however, no medications are directly administered through the spinal needle [52]. The spinal needle is withdrawn, and the epidural catheter inserted and dosed with a conventional dose (12–20 mL) of dilute local anesthetic (eg, bupivacaine 0.125%) with or without an opioid (fentanyl 2 μg/mL). Following their landmark study in 2008, investigators at the Brigham and Women's Hospital [2] coined the name and acronym DPE for the technique and popularized its use in obstetric patients.

Translocation

In 1996, Suzuki and colleagues [10] observed that an EPL with a 26-gauge dural puncture, compared with a conventional EPL, improves the caudal spread of epidural anesthesia in lower abdominal surgical patients. The improvement in the spread of anesthesia was attributed to a small amount of epidural medication flowing into the intrathecal space, or translocating via the dural puncture. Translocation is thought to be the principal mechanism responsible for the benefits observed with the DPE technique in subsequent clinical trials.

Leach and Smith [53] provided the first radiographic evidence of medication translocation from the epidural to intrathecal space. In a postpartum patient who experienced an inadvertent dural puncture, contrast dye solution injected through the epidural catheter was observed to spread into the spinal space. The study raised the concern for a high or total spinal blockade with epidural catheter dosing after an accidental dural puncture, or potentially even after a routine CSE technique.

Effect of dural puncture size

Based on the laws of physics, the size of the dural perforation should be directly proportional to the transdural flux of medications passing per unit time. Although the transdural flux from a dural puncture with an epidural needle would be significant, the transdural flux from a smaller gauge spinal needle should be much less. Bernards and colleagues [54] investigated the relationship between needle size and flux of morphine and lidocaine through spinal meningeal tissues of anesthetized monkeys mounted in a diffusion cell. Meningeal tissue puncture with a 27-gauge Whitacre, a 24-gauge Sprotte, and an 18-gauge Tuohy needle resulted in a significant and positive correlation between perforation size and flux across the tissue. Moreover, for drugs that have high flux across intact tissues (eg, lidocaine), translocation does not contribute significantly to total flux with small dural punctures (ie, 27 gauge). By contrast, for drugs that have slow flux across intact tissues (eg, morphine), translocation contributes significantly to net drug transfer across the tissue (Fig. 1). As a consequence, for the DPE technique to offer any difference compared with the EPL with local anesthetic agents, the spinal needle used to create the dural puncture should be larger than 27 gauge.

Findings from clinical studies are consistent with the in vitro report that concluded flux depends on the size of dural puncture and that a 27-gauge needle offers no significant transdural flux compared with intact tissue for local anesthetics (Table 2). Thomas and colleagues [55] conducted the first randomized study using the DPE technique within the obstetric population. Healthy laboring parturients requesting neuraxial labor analgesia were assigned to receive EPL or DPE techniques using a 27-gauge Whitacre needle for dural puncture and a total of 10 mL of 2% plain lidocaine for the initial dose. The investigators found virtually no differences between the two groups in labor analgesia quality, catheter manipulation, and catheter replacement rates. By contrast, subsequent studies using larger 25-gauge and 26-gauge Whitacre needles found faster onset to analgesia and better sensory block characteristics [2,56] with the DPE technique [1–3].

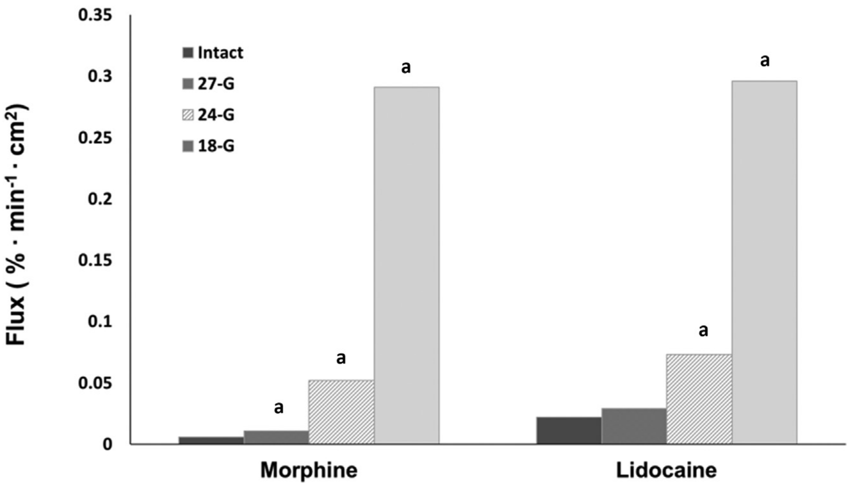

Fig. 1. Animal model of morphine and lidocaine flux though intact and punctured meningeal tissues. Compared with flux through intact tissue, significant difference was found at the 27-gauge (G) dural perforation with morphine, but not lidocaine. [a] $P<.05$. (*Data from* Bernards CM, Kopacz DJ, Michel MZ. Effect of needle puncture on morphine and lidocaine flux through the spinal meninges of the monkey in vitro. Implications for combined spinal-epidural anesthesia. Anesthesiology 1994;80:853–8.)

Effect of initial epidural loading volume and local anesthetic concentration

Administration of solution into the epidural space results in simultaneous increase in both subarachnoid and epidural pressures as the volume of the epidural solution compresses the spinal space [57,58]. This volume effect, seen also in studies examining the EVE technique, is an important element in enhancing translocation and thus the block properties of the DPE technique. Cappiello and colleagues [2] prospectively randomized 80 parturients in early labor requesting neuraxial analgesia to receive a DPE (using a 25-gauge Whitacre needle) or EPL. Using a total volume of 12 mL of 0.25% bupivacaine for the initial epidural loading dose, a significantly greater number of patients had S1 blockade at 20 minutes in the DPE group (36 vs 28, $P = .02$). Although there were also more patients in the DPE group who had symmetric block (36 vs 30, $P = .07$) and achieved visual analog scale (VAS) less than 10 at 20 minutes (33 vs 26, $P = .07$), these did not achieve statistical significance [56]. These findings led the same investigators to launch a subsequent study using a higher volume and less concentrated solution to determine whether the volume effect could be optimized. Chau and colleagues [1,52] prospectively randomized parturients to receive DPE, CSE, or EPL (with a 25-gauge Whitacre needle for the DPE and CSE techniques) and used a total of 20 mL of 0.125% bupivacaine for the epidural loading dose for the DPE and EPL. There were several important findings. First, compared with the EPL, the DPE technique had significantly earlier and greater incidence of bilateral

Table 2
Summary of randomized clinical trials using the dural puncture epidural technique in obstetric patients

Study	Spinal needle used	Initial epidural volume	Initial epidural solution	Primary outcome	Result
Thomas et al [55], 2005	27-gauge Whitacre	10 mL	2% plain lidocaine	Epidural catheter manipulation rates	No difference • 37.4% DPE vs 27.6% EPL ($P = .12$)
Cappiello et al [2,56], 2008	25-gauge Whitacre	12 mL	0.25% plain bupivacaine	Presence of sacral (S1) blockade and VAS<10 within 20 min of initiation of epidural analgesia	DPE>EPL • 92.3% DPE vs 70% EPL ($P = .02$)
Chau et al [1], 2017	25-gauge Whitacre	20 mL	0.125% plain bupivacaine + 40 µg fentanyl	Time to NPRS ≤1	CSE>DPE = EPL • DPE vs CSE: HR 0.36 (95% CI, 0.22–0.59, $P = .0001$) • No difference between EPL and DPE: HR 1.4 (95% CI, 0.83–2.4, $P = .21$)
Wilson et al [3], 2018	26-gauge Whitacre	15 mL	3 mL 1.5% lidocaine with epinephrine 5 µg/mL, then 12 mL 0.125% bupivacaine + 50 µg fentanyl	Proportion of patients with VAS ≤10 mm at 10 min	No difference • 55.3% DPE vs 44.7% EPL ($P = .26$)

Abbreviations: CI, confidence interval; HR, hazard ratio; NPRS, numeric pain rating scale; VAS, visual analog scale.

S2 blockade at 10 minutes (risk ratio [RR], 2.13; 95% CI, 1.39–3.28; $P<.01$), 20 minutes (RR, 1.60; 95% CI, 1.26–2.03; $P<.001$), and 30 minutes (RR, 0.19; 95% CI, 0.07–0.51; $P<.001$). Second, despite evaluating the largest initial epidural volume (20 mL) among all the DPE investigations within the obstetric population, the median (range) peak sensory block heights at 30 minutes and throughout the labor were similar between all 3 techniques (EPL T4 [T2–T8], DPE T4 [T2–T8], CSE T4 [T2–T6]). Third, a novel and important workforce implication of this study was the fewer physician top-up interventions found with the DPE technique, compared with both CSE and EPL groups (RR, 0.45; 95% CI, 0.23–0.86; $P = .011$). The transition from spinal to epidural analgesia observed with the CSE technique and the greater one-sided and patchy analgesia observed in the EPL were likely responsible for the difference in top-up interventions compared with the DPE technique.

Comparison of different neuraxial techniques

Onset of analgesia

Compared with CSE and EPL, the DPE technique has an intermediate onset of action. Chau and colleagues [1] found that the median (interquartile range [IQR]) time to adequate analgesia, defined as numeric pain rating scale (NPRS) less than or equal to 1 following administration of intrathecal bupivacaine 1.7 mg and fentanyl 17 μg (ie, 1 mL of a 1.5 mL premix solution of 0.25% bupivacaine and fentanyl 25 μg) for the CSE technique or epidural administration of 20 mL of 0.125% bupivacaine and fentanyl 2 μg/mL for the DPE and EPLs were 2 (0.5–6) minutes for CSE, 11 (4–120) minutes for DPE, and 18 (10–120) minutes for the EPL. In a recent study by Wilson and colleagues [3], DPE (26-gauge Whitacre) also had a faster onset compared with the EPL; the median times (95% CI) to VAS less than or equal to 10 mm were 8 (6–10) minutes versus 10 (8–14) minutes, respectively.

Sacral blockade

Despite a well-sited epidural catheter and an appropriate volume and concentration of local anesthetic given, sensory blockade may not spread to the sacral dermatome. This problem is known as sacral sparing and is seen commonly with EPL. Patients with sacral sparing typically complain of increased somatic pain and pressure in the perineal area (S2–S4 nerve root distribution) during the second stage of labor. Sacral nerve roots and fibers are larger in diameter, located more caudally, and are surrounded by thick dura mater [59]. Fluoroscopic studies of the epidural space have shown that, following administration of epidural solution in the lower lumbar segments, there is greater distribution of the solution in the cephalad, compared with the caudad, direction [60,61]. By contrast, direct administration into the CSF allows the medication solution to spread more easily cephalad and caudad within the liquid medium of the intrathecal space, and medications can directly reach the nerve roots, yielding significantly faster onset and superior sacral coverage compared with EPL [62]. Clinically, more parturients have relief of painful rectal pressure with CSE versus EPL (94.8% vs 68.7%; $P<.0001$) [62]. The DPE technique does not result in the same amount of intrathecal drug spread in the CSF compared with the CSE technique but harnesses both the epidural and spinal space in the same manner to improve caudal spread. Using 25-gauge and 26-gauge Whitacre needles, multiple investigators have found the DPE technique to result in earlier and greater caudal spread compared with EPL [1,2,10]. In the study by Chau and colleagues [1] comparing DPE, CSE, and EPL, 100% of the patients in the DPE and CSE groups achieved S2 blockade at 20 minutes; however, 5% of the patients in the EPL group never experienced S2 blockade for the entire duration of labor.

Failed epidural conversion

One of the concerns with tradition EPL is the potential failure to rapidly and reliably convert the labor analgesia to surgical epidural anesthesia for cesarean delivery, thus necessitating induction of general anesthesia [63]. The reported incidence of failed epidural conversion in the literature is wide, ranging from 0% to as high as 21%. However, the rate of failure can be influenced by the definitions of failure used, institutional practice, urgency of the delivery, and accuracy of reporting. In a systematic review and meta-analysis of 13 studies with more than 8600 patients by Bauer and colleagues [64], the incidence of cesarean deliveries performed under general anesthesia in women with in situ epidural catheters was 5% (95% CI, 3.5%–6.5%), and the need for a second anesthetic (including spinal, repeat EPLs, or general anesthesia at the time of cesarean delivery) was 7.7% (95% CI, 5.0%–10.5%).

Many risk factors have been reported in retrospective studies to be associated with failed epidural conversion. Some of the strongest predictors include urgency of operative delivery (odds ratio [OR], 40.4; 95% CI, 8.8–185.6), number of epidural top-up boluses and having higher VAS pain score in the 2 hours before cesarean delivery (OR, 4.39; 95% CI, 1.6–12.2) [65], greater than 2 breakthrough pain episodes (OR, 6.65; 95% CI, 2.48–17.87) [66], and generalist anesthesiologist versus an obstetric anesthesiologist providing care (OR, 4.76; 95% CI, 1.5–15.6) [67].

As many other areas in medicine, prevention is the key to avoiding a failed epidural conversion. The use of adjuncts such as fentanyl and bicarbonate may improve the onset and quality of sensory block of lidocaine or 2-chloroprocaine when time is critical. Prompt management and replacement of a poorly functioning catheter and close communication with nursing and obstetric teams provide more time for the provider to optimize the catheter function. There are insufficient data to support one neuraxial initiation technique over another to prevent failed epidural conversion. One retrospective study found EPL had higher failed epidural conversion compared with the CSE technique (OR, 5.54; 95% CI, 2.07–14.85) [66]; however, this finding was not replicable in other studies [68–70]. There are also initial data suggesting that dural puncture without intrathecal medication (ie, DPE technique) leads to improved spread and reliable analgesia; whether this may also apply to surgical anesthesia has not been investigated.

When a failed epidural conversion occurs, the catheter may be rescued by giving a rebolus of medications of sufficient concentration and volume (10 mL); withdrawing the catheter back 1 cm and providing a rebolus of medications has a similar success rate. There is evidence that obstetric anesthesiologists, compared with generalists, are more likely to attempt a catheter rescue technique [67,71]. In one study, 85% of the failed epidural catheters were rescued using the catheter withdrawal technique [67]. If this is unsuccessful, and time is not critical, an alternative neuraxial technique should be attempted. Repeating the EPL may not overcome any anatomic problem that led to the failure. Further volume may complicate alternative neuraxial techniques. Single-shot spinal anesthesia following failed epidural conversion with large volumes of local anesthetic in the epidural space may risk high or total spinal anesthesia [72–74]. Some clinicians recommend decreasing the intrathecal dose, but the optimal dose is not known. The DPE or sequential CSE techniques may be more appealing options in this scenario, because they harness both the spinal and epidural spaces to augment and extend the epidural block.

Catheter replacement

Heesen and colleagues [75] conducted a meta-analysis of 10 randomized trials with more than 1700 parturients and found the relative risk of catheter replacement was similar after CSE versus EPL (RR, 0.57; 95% CI, 0.32–1.03; $P = .37$). However, prospective and retrospective clinical studies have shown that epidural catheters inserted as part of a CSE technique with CSF return through the spinal needle, compared with absence of CSF, are less likely to fail and require fewer replacement attempts. Grondin and colleagues [76] found that an epidural catheter placed as part of a CSE technique that did not have CSF return through the spinal needle had significantly higher rate of catheter replacement (28.6% vs 4.1%; $P < .03$). Thomas and colleagues [55] found no difference between catheter replacement rates between EPL versus DPE using a 27-gauge Whitacre (9.3% vs 8.1%; $P = .82$). However, in a subgroup of 18 patients who had a dural puncture with no CSF return through the spinal needle, the overall epidural catheter replacement rate increased to 22%. The return of CSF through the spinal needle in the DPE and CSE technique gives providers additional reassurance that the epidural needle is midline and correctly placed in the epidural space.

Block symmetry

Incomplete (patchy) or asymmetric blockade can occur up to 8% of the time [77,78]. Most providers rescue an asymmetric blockade by giving more volume in the epidural space. A meta-analysis found the relative risk of unilateral block was significantly reduced after CSE versus EPL (RR, 0.48; 95% CI, 0.24–0.97; $P = .01$) [75]. One explanation is that a successful dural puncture with CSF return can indicate that the tip of the epidural needle is midline. In addition, translocation into the spinal space and subsequent spinal analgesia may play a role in compensating for an incomplete spread in the epidural space.

Post–dural puncture headache

There are concerns that a CSE or DPE technique may increase the risk of PDPH; however, this concern has not been borne out by evidence. Large retrospective studies have shown similar rates of PDPH and epidural blood patch use in parturients who received EPL or CSE techniques for labor analgesia [79–81]. There are several possible explanations for this finding. First, the epidural catheter and volume of local anesthetic solution in the epidural space may increase the epidural pressure and thus protect the parturient against excessive efflux of CSF. Second, dural puncture with a spinal needle may decrease accidental dural puncture (ADP) by the larger epidural needle. When loss of resistance is equivocal, the provider may advance the epidural needle and risk ADP or pass a spinal needle to obtain additional information on the location of the tip of the epidural needle. Return of CSF helps to differentiate between a true from a false loss of resistance. Return of CSF also helps to minimize epidural catheter replacement, as discussed earlier, and thus avoid risk of ADP that may occur during a repeat procedure.

Uterine tachysystole and fetal bradycardia

Although CSE clearly has a superior speed of onset compared with the other techniques, the administration of intrathecal opioids has been associated with increased incidence of uterine tachysystole and fetal bradycardia [82]. Although the exact mechanism is unclear, one theory is that it may be related to changes or imbalance in serum catecholamine levels following neuraxial placement. Earlier studies have reported significant reduction in plasma epinephrine with minimal change or slight increase in plasma norepinephrine level after labor analgesia compared with pre-analgesia values [83,84]. Clarke and colleagues [82] proposed that the decrease in epinephrine levels, which has a tocolytic effect via beta-2 adrenoreceptor agonism, leads to unopposed increase in uterine tone, which in turn leads to decreased placental blood flow and fetal bradycardia. By contrast, Riley [85] proposed that increased norepinephrine level may lead to uterine artery vasoconstriction, which in turn leads to decrease placental blood and fetal bradycardia. Neither hypotheses have been definitively proven. However, concerns over inciting uterine tachysystole have led some providers to decrease the dose of intrathecal opioid administered or avoid performing the CSE technique altogether [86].

The DPE technique does not involve direct intrathecal opioid administration, and this decreases the speed of onset but also significantly decreases the incidence of uterine tachysystole and hypertonus compared with the CSE technique (RR, 0.22; 95% CI, 0.08–0.60; $P < .001$) [1]. The faster CSE technique has a higher probability of uterine hypertonus and fetal heart rate changes that may put the fetus at greater risk [87]. The DPE technique may improve the speed of onset compared with EPL without a significant increase in adverse effect on the uterine contractility and fetal heart rate (Table 3).

Table 3
Comparison of techniques for initiation of neuraxial labor analgesia

	CSE	DPE	EPL
Block Characteristics			
Median (IQR) Time to NPRS ≤1 (min)	Rapid 2 (0.5–6)	Intermediate 11 (4–120)	Slow 18 (10–120)
Caudal Spread	Earlier, increased spread	Earlier, increased spread	Delayed, or sacral block sparing
Cephalad Spread >T4 Dermatome Level Following Initial Loading Dose	Low risk	Low risk	Low risk
Catheter Testing Following Placement	Delayed	Immediate	Immediate
Block Symmetry	Higher	Higher	Lower
Failed Block	Lower risk with CSF return	Lower risk with CSF return	Higher risk
Incidence of Adverse Effects			
Pruritus	Higher	Lower	Lower
PDPH	No difference	No difference	No difference
Motor Block	Lower	Lower	Higher
Transition of Analgesia	Present	Absent	Absent
Catheter Replacement Rate	Lower	Lower	Higher
Uterine Tachysystole	Higher	Lower	Lower
Fetal Bradycardia	Higher	Lower	Lower
Emergency Cesarean delivery Caused by Fetal Bradycardia	No difference	No difference	No difference

Abbreviations: IQR, interquartile range; NPRS, numeric pain rating scale.

TECHNIQUES FOR MAINTENANCE OF NEURAXIAL LABOR ANALGESIA

Once neuraxial labor analgesia is initiated, maintenance of analgesia can be achieved with a number of techniques. One technique is to treat breakthrough pain using intermittent manual top-ups by the anesthesia provider or PCEA by the patient. Another technique is to prevent pain from recurring using continuous infusions (CEI) or PIEB.

When EPL was first introduced for labor analgesia, manual intermittent boluses of local anesthetics were administered by midwives or anesthesia providers [88]. A large volume of concentrated local anesthetic solution was usually administered so that onset could be more rapid and the frequency of providers having to rebolus was minimized. This form of breakthrough pain relief was inconsistent and suboptimal; patients experiencing pain had to have anesthesia providers available, and, once analgesia was administered, many developed motor blockade.

Patient-controlled epidural analgesia

Introduced by Gambling and colleagues [89] in 1988, PCEA is a popular technique for maintenance of neuraxial labor analgesia because it enables parturients to individualize their own analgesia [90].

Compared with CEI alone, the use of PCEA alone has been shown to decrease anesthetic consumption, decrease clinician intervention, and decrease motor block [90,91]. The addition of PCEA to CEI was found to decrease unscheduled clinician intervention without increasing anesthetic consumption [92]. This finding of reduced workload has resulted in many centers adopting this combined technique for maintenance of labor analgesia. However, even with CEI plus PCEA, some patients still experience breakthrough pain, which has led to a series of investigations on further optimizing the PCEA pump settings.

There are significant variations in PCEA pump settings between institutions, reflecting the fact that no ideal pump settings have been determined [93]. Studies have examined adjusting the bolus volume or lockout intervals for labor [94–96]; the only consistent finding is that large bolus doses of dilute local anesthetic improve analgesia and maternal satisfaction compared with small boluses. Higher concentration of local anesthetic (eg, 0.25% bupivacaine or 0.2% ropivacaine) significantly increases the incidence of motor blockade [97].

Programmed intermittent epidural bolus

Almost 2 decades ago, Kaynar and Kodali [11] at Brigham and Women's Hospital reported their in vitro simulation experiment showing greater dye solution spread on a semiabsorbent paper with boluses compared with continuously infused solution through a multiorifice epidural catheter despite the same hourly volume being administered. This finding indicated that bolus administration generates greater pressure and spread within the epidural space; it promoted a concept that quickly led to the emergence of a series of investigations worldwide.

Multiple studies have consistently shown superiority of PIEB compared with CEI plus PCEA; the magnitudes of these outcomes are generally small. A 2013 systematic review and meta-analysis [98] of 9 randomized trials found that, compared with CEI, PIEB use results in lower local anesthetic consumption (median difference (MD), −1.2 mg bupivacaine equivalent per hour; 95% CI, −22 to −0.3), shorter duration of second stage of labor (MD −12 minutes; 95% CI, −23–0), and higher maternal satisfaction on a 100-mm VAS (MD, 7.0 mm; 95% CI, 6.2–7.8). Other studies have also found decreased clinician intervention [99,100], increased time to first rescue bolus [99,101–104], and fewer manual boluses with PIEB versus CEI [99,105,106] (Table 4).

Table 4
Comparison of techniques for maintenance of neuraxial labor analgesia

	CEI + PCEA	PIEB + PCEA
Hourly Local Anesthetic Consumption	Higher	Lower
Hourly Opioid Consumption	Higher	Lower
Duration of Second Stage of Labor	Longer	Shorter
Instrumental Vaginal Delivery Rate	Higher	Lower
Maternal Satisfaction	Lower	Higher
Clinician Intervention	Higher	Lower
Time to First Rescue Bolus	Higher	Lower
Manual Bolus	Higher	Lower

One study found significant reduction in instrumental delivery rates with PIEB compared with CEI (7% vs 20%; $P = .03$) [107]. Although the study was powered to examine this secondary outcome, this finding has not been replicated in other studies and the decision to perform instrumental delivery is difficult to control as a confounder because it is influenced by individual obstetrician's practice and comfort with the procedure.

The optimal PIEB pump settings have been the subject of intense investigation over the last decade. Three variables have been the recent focus of these investigations: (1) PIEB bolus interval, (2) PIEB bolus volume, and (3) pump flow rate. Carvalho and colleagues [112] at the University of Toronto conducted a series of biased-coin up-down sequential allocation studies to determine the optimal PIEB bolus interval and volume. Epsztein Kanczuk and colleagues [108] studied 40 parturients using PIEB 10 mL of 0.0625% bupivacaine with fentanyl 2 μg/mL and estimated that the effective interval to produce analgesia in 90% of women during the first stage of labor is approximately 40 minutes. Using this information, Zakus and colleagues [109] studied another 40 parturients using the same local anesthetic solution with 40 minutes as the PIEB bolus interval to estimate the effective bolus volume to produce analgesia in 90% of women during the first stage of labor. The estimated bolus volume was approximately 10 to 11 mL and it was not possible to reduce the PIEB volume to less than 10 mL without compromising quality of analgesia.

A recent study examined the effect of bolus delivery rate (ie, pump flow rate) on maintenance of labor analgesia. High flow rate may generate higher injectate pressure and thus improve drug spread in the epidural space. Lange and colleagues [110] randomized 220 parturients to PIEB plus PCEA with high (300 mL/h) or low flow rate (100 mL/h) and recorded the proportion of subjects in each group who had breakthrough pain requiring a clinician intervention. There were fewer provider-administered supplemental boluses in the high-rate group, but this was similar to the low-rate group (36.3% vs 40.7%, difference −4.4%; 95% CI, −18.5%–9.1%; $P = .69$). Other outcomes, including time to first request for supplemental analgesia, pain score, and patient satisfaction scores, were similar between the two groups. Another recent retrospective impact study compared 140 parturients receiving PIEB with low (250 mL/h) versus high flow rate (500 mL/h) and also found no difference in the clinician top-up intervention rate between the two groups [111]. These studies all used single-orifice epidural catheters; whether a multiorifice epidural catheter would yield similar results is currently unknown.

One potential safety concern with the PIEB technique is delayed recognition of a mispositioned epidural catheter. Specifically, a few early adopters of the PIEB technique reported unrecognized intrathecal catheter insertion following a CSE technique with no test doses administered. On the next programmed bolus, the patients inadvertently received bolus doses into the intrathecal space; depending on the volume and concentration, a high and total spinal anesthesia may ensue. Other potential concerns have included hypotension, motor block, and epidural pump occlusion; however, most institutions that have changed to the PIEB regimen have not reported concerning risks.

IMPLEMENTATION OF PROGRAMMED INTERMITTENT EPIDURAL BOLUS FOR MAINTENANCE OF LABOR ANALGESIA

Many centers are now adopting the PIEB regimen, especially given the overwhelming evidence of benefit compared with the CEI regimen and that pumps capable of PIEB and PCEA functions are now available. For centers considering a switch, there are several issues that need to be considered. Cost is a notable factor, but, if new pumps are to be purchased anyway, PIEB pumps may represent a better value compared with CEI pumps. If new CEI pumps were recently purchased, replacing them would incur a significant expense. In some cases, a software upgrade may be all that is required. Many centers are using lower flow rates (100–250 mL/h); higher flow rates (ie, 500 mL/h) require disposable high-volume tubing to be purchased otherwise the pump may indicate an occlusion [112]. In addition, education of anesthesiologists, obstetricians, midwives, nursing staff, and trainees is required before implementation to discuss new terminologies and settings in specific PIEB pumps (Table 5). Development of protocols and order sheets also needs to occur at the hospital management level. Ongoing quality improvement initiatives should also be developed so that pump settings, work flow, and education strategies can all be reviewed on a regular basis to optimize efficacy and safety.

FUTURE DIRECTIONS AND OPPORTUNITIES FOR RESEARCH

There are several unanswered questions with the neuraxial labor analgesia initiation and maintenance techniques. Research on the DPE technique lags behind that of EPL and CSE techniques because of its recent adoption into clinical practice. The DPE investigations to date have primarily focused on analgesia outcomes shortly after the initiation of labor analgesia; further investigations are needed to understand differences from CSE and EPL during

Table 5
Programmed intermittent epidural bolus pump parameters, definitions, and common setting ranges

Parameters	Definition	Common Settings
Next bolus interval	Time from the start of pump to first PIEB bolus volume	30–60 min
PIEB bolus volume	Volume delivered per bolus	5–10 mL
PIEB bolus interval	Time from one PIEB volume bolus to the next PIEB volume bolus	45–60 min
Clinician bolus	Bolus volume administered by clinician	5–10 mL
PCEA Bolus	Bolus volume administered by patient	5–10 mL
Lock-out interval	Time from one PCEA dose to the next PCEA dose	10–15 min
Pump flow rate	Rate of PIEB bolus delivered	250–500 mL/h

the labor analgesia maintenance phase, including with the recently adopted PIEB settings.

The ideal PIEB parameters (including pump flow rates) have not been determined. There are recent studies on optimal bolus interval and flow rates, but further studies are required. Whether DPE and PIEB can be synergistic with each other in providing improved labor analgesia is not currently known; there are at least theoretic reasons to believe that the PIEB settings may further encourage translocation. Although there do not seem to be any safety concerns with PIEB, there is also very little published information on the use of PIEB in selected populations such as patients with pseudotumor cerebri or those with reduced epidural space compliance. Further studies will help address these questions.

Ongoing investigations and desires to investigate improved techniques to optimize the labor experience for parturients will lead to further refinement and development of exciting new neuraxial techniques. The development of novel initiation or maintenance techniques may not replace older ones but increase the armamentarium of obstetric anesthesiologists in managing different patients in a variety of contexts.

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