

CME

Continuous Peripheral Nerve Blocks: A Review of the Published Evidence

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A continuous peripheral nerve block, also termed “perineural local anesthetic infusion,” involves the percutaneous insertion of a catheter adjacent to a peripheral nerve, followed by local anesthetic administration via the catheter, providing anesthesia/analgesia for multiple days or even months. Continuous peripheral nerve blocks may be provided in the hospital setting, but the use of lightweight, portable pumps permits ambulatory infusion as well. This technique’s most common application is providing analgesia after surgical procedures. However, additional indications include treating intractable hiccups; inducing a sympathectomy and vasodilation to increase blood flow after a vascular accident, digit transfer/replantation, or limb salvage; alleviating vasospasm of Raynaud disease; and treating peripheral embolism and chronic pain such as complex regional pain syndrome, phantom limb pain, trigeminal neuralgia, and cancer-induced pain. After trauma, perineural infusion can provide analgesia during transportation to a distant treatment center, or while simply awaiting surgical repair. Catheter insertion may be accomplished using many possible modalities, including nerve stimulation, ultrasound guidance, paresthesia induction, fluoroscopic imaging, and simple tactile perceptions (“facial click”). Either a nonstimulating epidural-type catheter may be used, or a “stimulating catheter” that delivers electrical current to its tip. Administered infusate generally includes exclusively long-acting, dilute, local anesthetic delivered as a bolus only, basal only, or basal-bolus combination. Documented benefits appear to be dependent on successfully improving analgesia, and include decreasing baseline/breakthrough/dynamic pain, supplemental analgesic requirements, opioid-related side effects, and sleep disturbances. In some cases, patient satisfaction and ambulation/functioning may be improved; an accelerated resumption of passive joint range-of-motion realized; and the time until discharge readiness as well as actual discharge from the hospital or rehabilitation center achieved. Lastly, postoperative joint inflammation and inflammatory markers may be decreased. Nearly all benefits occur during the infusion itself, but several randomized controlled trials suggest that in some situations there are prolonged benefits after catheter removal as well. Easily rectified minor complications occur somewhat frequently, but major risks including clinically relevant infection and nerve injury are relatively rare. This article is an evidence-based review of the published literature involving continuous peripheral nerve blocks. (*Anesth Analg* 2011;113:904–25)

Continuous peripheral nerve blocks (CPNBs) are relatively simple in concept: a catheter is percutaneously inserted adjacent to a peripheral nerve, followed by local anesthetic administration via the catheter (Fig. 1). Thus, the terms CPNB and “perineural local anesthetic infusion” are often used synonymously. Using currently available long-acting local anesthetics, the maximal duration of a single-injection peripheral nerve block is 8 to 24 hours. Therefore, CPNB provides an alternative option when a prolonged neural blockade is desired.^{1,2} Since its first description in 1946,³ CPNB has evolved from an experimental case report involving a needle inserted through a cork taped to a patient’s chest, to a well-validated analgesic technique accepted by the medical community

with products designed solely for its application. This article is an evidence-based review of the published CPNB literature.

INDICATIONS

The earliest reports of CPNB describe prolonging intraoperative surgical anesthesia^{3,4} and treating intractable hiccups.⁵ Later articles report using CPNB-induced sympathectomy and vasodilation to increase blood flow after a vascular accident,⁶ digit transfer/replantation,^{7,8} or limb salvage⁹; alleviate the vasospasm of Raynaud disease¹⁰; and treat peripheral embolism.¹¹ After trauma, CPNB can provide analgesia during transportation to a distant treatment center¹² or while simply awaiting surgical repair.¹³ Although yet unvalidated, reports describe CPNB to treat chronic pain, such as complex regional pain syndrome,¹⁴ intractable phantom limb pain,¹⁵ as well as pain from terminal cancer¹⁶ and trigeminal neuralgia.¹⁷ However, the overwhelming majority of CPNB reports involve the perioperative period, and only this application of perineural local anesthetic infusion remains validated with randomized controlled clinical trials (RCTs).¹⁸

Because there are intrinsic risks with CPNB, most providers restrict its use to surgical procedures that are expected to result in pain not easily controlled with less-invasive analgesic techniques (e.g., oral analgesics, cooling/heating pads)¹⁹ or in

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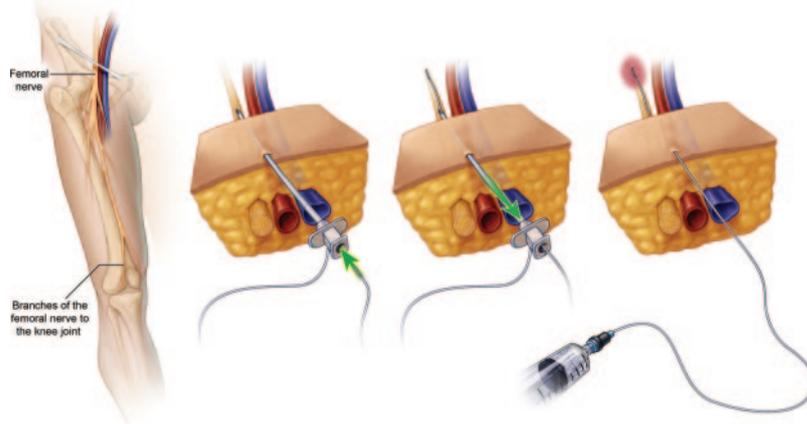
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Figure 1. Illustration of a continuous peripheral nerve block involving the femoral nerve. This particular perineural catheter insertion technique employs electrical stimulation alone *via* a stimulating catheter.



patients with an intolerance to alternative analgesics (e.g., opioid-induced nausea).^{20,21} The surgical site dictates the anatomic location of catheter insertion (Table 1). Although not as thoroughly validated as in adults, CPNB has been described in hundreds of pediatric patients.^{14,22–27}

CATHETER INSERTION (NERVE STIMULATION)

Historically, perineural catheters were inserted using induced paresthesia,³ a facial “click,”²⁸ or fluoroscopic guidance.²⁹ However, after the introduction of portable nerve stimulators in the 1970s, the overwhelming majority of published CPNB reports involve this modality. Originally, this technique involved using electrical current to place an insulated needle adjacent to a peripheral nerve, followed by injection of local anesthetic and subsequent perineural catheter insertion. Although multiple prospective studies document the possible high success rate of this procedure,^{30–33} others have found an unacceptably high rate of “secondary block” failure,³⁴ presumably when the catheter tip was unknowingly misplaced during insertion.³⁵ To help counter this risk, the perineural catheter may be first inserted, followed by a local anesthetic bolus via the catheter itself.^{36–39} However, remaining unknown is whether a relatively large bolus of concentrated local anesthetic resulting in a successful nerve block guarantees that the catheter tip is close enough to the target nerve(s) to provide analgesia during the subsequent infusion with relatively small volumes of dilute local anesthetic. Regardless, even if prediction of successful perineural infusion is provided, the identification of those failed catheters requires waiting at least 15 minutes for block onset/failure, followed by removal of the catheter/dressing, reparation, and catheter reinsertion, a process requiring a longer period of time than many practices permit.⁴⁰ In addition, a partial block is possible, suggesting the catheter tip is not optimally located, but often precluding replacement using electrical current.

An option is the use of a “stimulating catheter” in which an electrical current is used with an insulated needle to locate the target nerve(s), followed by the insertion of a perineural catheter that conducts current to its tip.^{19,41,42} If muscle contraction intensity decreases during catheter advancement, it is presumed that the catheter tip is moving

away from the target nerve.⁴³ This provides real-time evidence of catheter-nerve distance.⁴⁴ There are data to suggest that in the area of the popliteal fossa, using stimulation during catheter advancement results in the catheter tip being placed closer to the sciatic nerve.^{45–48} Although there are limited data suggesting a similar improvement for femoral and interscalene catheters,^{43,49,50} the clinical relevance is questionable for these anatomic locations.^{51–56}

Unfortunately, continuous muscle contraction guarantees neither surgical block nor postoperative infusion success.^{43,57–59} In addition, adequate muscle response cannot always be elicited with catheter advancement^{43,59–64}; and stimulating catheters take more time on average for placement and cost more than their nonstimulating counterparts,^{48,65} leading some to question their overall benefit.⁶⁶ There is minimal,⁶⁷ if any, benefit of injecting fluid via the needle before catheter insertion to “open” the perineural space,⁶⁸ but D5W is recommended if a bolus is used.^{69,70} Lastly, there are few data to provide recommendations on the minimal acceptable current resulting in a muscle response.⁷¹

The optimal distance to advance a perineural catheter past the needle tip remains unknown, but there are data to suggest that increasing the insertion distance is correlated with an increased risk of catheter coiling, and possibly the final nerve-to-catheter tip distance.^{36,72–74} Considering the multiple catheter knots reported with insertion >5 cm,^{75–78} and the lack of data suggesting insertion lengths >5 cm is beneficial, recommending a maximal insertion of 5 cm seems warranted.⁶⁶ Recently reported “self-coiling catheters” may render this issue moot in the future if they are found reliable and approved for human use.⁷⁹ Similarly, the optimal minimum insertion distance remains unknown, with evidence that 0 to 1 cm results in a minimal risk of secondary block failure,^{33,80} but possibly an increased risk of subsequent dislodgement.⁸¹

CATHETER INSERTION (ULTRASOUND)

Unfortunately, data from controlled trials involving electrical stimulation-guided catheter insertion, or even ultrasound-guided single-injection blocks, is not automatically applicable to ultrasound-guided catheter insertion for

Table 1. Catheter Locations

Surgical site	Major approaches	Evaluated with RCT?	Comments	Comparative CPNB studies
Head	Mandibular and maxillary nerves Interscalene	No ^{1,7,324,325} Yes ^{34,93,173,178,217,230,326-331}	Validated with nerve stimulation ^{34,38,173,178,217,230,326-328} and ultrasound guidance ^{93,329}	There are no studies comparing these CPNB techniques.
Shoulder and proximal humerus	Cervical paravertebral Intersternocleidomastoid Supraclavicular	No ³³² No ³³³ No ^{232,233}	Nearly all publications from a single group Effectiveness of technique for postoperative analgesia unclear without RCT	
Elbow, forearm, and hand	Suprascapular Supraclavicular Infraclavicular Axillary	No ³³⁴ Yes ²³¹ Yes ²²⁷ Yes ^{153,a}	Effectiveness of technique unclear without RCT Caution regarding pneumothorax risk ³³⁵ (including with ultrasound guidance) ³³⁶	Infraclavicular provides superior analgesia to both supraclavicular ²³¹ and axillary ^a catheters
Thorax and breast	Median nerve Paravertebral	No ³³⁷ Yes ^{338,339}	No benefit of ropivacaine 0.1% or 0.2% over placebo infusion	
Abdomen, iliac crest, and inguinal region	Intercostal Transversus abdominus plane	No ^{340,341} No ^{234,342-345}	For mastectomy: no infusion benefits over single injection. ³³⁸ For open lung surgery: benefits over thoracic epidural. ³³⁹ Approach aims to place catheter tip in paravertebral space. Effectiveness of this technique unclear without RCT. Relatively new technique with risks and benefits yet to be thoroughly investigated. Retrospective study suggests decreased opioid requirements and pain scores in renal transplant recipients. ³⁴⁵	There are no studies comparing these CPNB techniques
Hip and thigh	Posterior lumbar plexus Femoral Parasacral	Yes ^{13,33,213,236,346-348} Yes ^{213,237,242,346,349,350} No ³⁵¹	Impact of various catheter insertion techniques remains uninvestigated. Surgery involving the posterior thigh: reliable analgesia for the posterior femoral cutaneous nerve distribution	For hip arthroplasty, patients with femoral (versus posterior lumbar plexus) catheters: no difference in resting pain scores, but ambulation suffered ^{213,346} , dynamic pain scores either higher ³⁴⁶ or no difference ²¹³ , and increased opioid-related side effects and satisfaction ³⁴⁶
Knee and thigh	Posterior lumbar plexus Femoral	Yes ^{166,239,352} Yes ^{2,32,36,49,58,150,159,161,166,167,222,239,243,244,248,250,318,322,353-357}	Most frequently published catheter location for knee surgery. Impact of various catheter insertion techniques remains uninvestigated.	For knee arthroplasty, no major analgesic differences found among approaches ^{3,166,239,353,354}
Leg, ankle, and foot	Fascia iliaca Parasacral Labat and Raj Subgluteal Popliteal Tibial nerve Femoral	Yes ^{353,354,358,359} No ^{351,360} No ^{30,363} Yes ^{361,362} Yes ^{23,31,173,215,226} No ^{228,364} Yes ²⁴⁰	Reliable analgesia for the posterior femoral cutaneous nerve distribution Very few CPNB reports Most common continuous sciatic block published Femoral infusion in addition to, and not in place of, popliteal infusion for major ankle surgery	No major analgesic differences found between subgluteal and popliteal ^{361,362}

Only selected references are included because of publication limitations; similarly, only RCTs are included when at least 1 study with this design is available.
 RCT = randomized controlled trial; CPNB = continuous peripheral nerve block.
^a Unpublished data, Mariano and Iffled (2011).

multiple reasons. Although the limited length of this review article precludes an in-depth discussion of these issues, the information is available elsewhere.⁸² Whereas many relatively large series demonstrate the feasibility of ultrasound-guided catheter insertion,^{83–86} there are currently few RCTs to help guide practice.⁸⁷ One study suggests that for infraclavicular catheters, there is little difference in the surgical block resulting from a bolus of local anesthetic injected via the needle before catheter insertion compared with the catheter after needle removal.⁸⁸ Another RCT demonstrates the difficulty and poorer success rate of inserting a catheter with the longitudinal plane of the needle parallel to the femoral nerve compared with a perpendicular orientation.⁸⁹ Lastly, a recent publication suggests that for interscalene catheters, a needle with its long axis parallel to the nerve has distinct benefits compared with a perpendicular needle-to-nerve orientation.⁹⁰

Because of the multiple variables for various blocks/techniques (e.g., bolus via the catheter versus needle, catheter insertion distance, and catheter design), applying the results of one study to others' practices will most likely prove difficult.⁸² For example, the results of the above-mentioned infraclavicular catheter study will probably not be replicated with a single catheter injection of local anesthetic via a popliteal sciatic catheter because of differences in perineural anatomy between the 2 sites.⁹¹ Similarly, in the RCT comparing anterolateral and posterior approaches,⁹⁰ a relatively rigid 3-orifice catheter was used, greatly increasing the chance that for the posterior approach all 3 orifices would fail to reside within the narrow facial (anterior-posterior) plane containing the brachial plexus.⁹² Evidence from other investigations suggests that the posterior approach is highly reliable using a relatively flexible single-orifice catheter,^{62,93} and that using a flexible catheter for other needle in-plane approaches may help avoid the catheter tip bypassing the target nerve during insertion.^{74,81}

Simply visualizing the catheter tip in close relation to the target nerve intuitively seems to be an obvious solution; however, in practice, identifying the tip is often challenging because, unlike rigid needles, flexible catheters do not usually remain within the ultrasound plane of view. Although there are exceptions,^{94,95} many investigators observe the location of fluid,⁹⁶ an agitated fluid/air mixture,⁹⁷ or simply air^{98,99} injected through the catheter. Unfortunately, the positive and negative predictive value of each of these methods remains unknown, and even what constitutes a "positive" or "negative" test has yet to be determined. Future technological developments in equipment such as 3-dimensional ultrasound may render this issue moot.¹⁰⁰

NERVE STIMULATION VERSUS ULTRASOUND GUIDANCE

Many RCTs suggest that for most anatomic locations, catheters inserted with ultrasound guidance provide at least similar analgesia, and often decrease insertion-related discomfort and insertion time, compared with an electrical technique using an insulated needle and nonstimulating^{101–103} or stimulating catheters.^{61,62,64,104,105} And while there are reports of

combining nerve stimulation and ultrasound guidance for catheter insertion,^{43,106} the majority of these reports do not suggest much benefit^{93,97,104,107–109}—and often increasing difficulties compared with using one technique alone^{104,110,111}—leading some to question the utility of stimulating catheters,¹¹⁰ and even insulated needles¹¹² (while others disagree).^{19,56,106,113,114} Currently, insufficient data are available to determine the optimal techniques/equipment for these insertion modalities, and their associated risks and benefits.⁸² Case in point is 1 RCT providing contrary evidence that for popliteal-sciatic catheters, a stimulating catheter provides improved analgesia in those successfully placed using a strict insertion protocol.⁶³ Another RCT suggests that combining ultrasound guidance and nerve stimulation for catheter insertion leads to decreased local anesthetic consumption, opioid use, and pain scores.¹⁰⁶

There are some clinical situations in which ultrasound is a superior modality, at least theoretically, such as after limb amputation,¹¹⁵ when sensory nerves are solely targeted,¹¹⁶ with concomitant anticoagulation,¹¹⁷ or when an electrically induced muscle response is either undesirable¹¹⁸ or cannot be elicited.¹¹⁹ However, ultrasound nerve/plexus/needle-tip visualization/identification are often difficult for relatively deep targets, in which case nerve stimulation may prove beneficial.^{120–122} There are also situations, such as when placing a posterior lumbar plexus catheter, whereby prepuncture ultrasound visualization may aid subsequent electrical stimulation-guided catheter insertion.¹²³ Lastly, the relative costs of each insertion modality must be accounted for, with 1 investigation suggesting that for single-injection peripheral nerve blocks, the use of ultrasound guidance is at least as financially competitive, and often becomes a "profit center," depending on the clinical scenario, compared with electrical stimulation.¹²⁴

INFUSATES

Local anesthetic is the primary analgesic infused during CPNB. Although intermediate-duration drugs may be used,^{125,126} the most frequently reported drugs are ropivacaine, bupivacaine, and levobupivacaine because of their longer duration of action and favorable sensory:motor block ratio.¹²⁷ Because the precise equipotency ratios of perineural local anesthetics remain unknown, comparisons are problematic.¹²⁸ Although the available data suggest bupivacaine and levobupivacaine have higher potency than ropivacaine,^{129,130} all 3 provide similar analgesia within human trials. However, the ropivacaine concentration is often increased up to 50% to compensate for decreased potency.^{20,129–134} One study of interscalene infusion provides evidence that ropivacaine 0.2% induces fewer finger paresthesias and less hand weakness than bupivacaine 0.15%.¹³³ However, similar investigations using different concentrations of levobupivacaine and ropivacaine suggest that any differences in the induced motor block are minimal as long as the ropivacaine concentration is increased by approximately 50%.^{129–132} Conversely, there are data to suggest that when the perineural infusion is discontinued, the sensory and motor effects of bupivacaine greatly outlast those of ropivacaine.¹³³ This may be relevant when titration of local anesthetic to limit undesired effects

is needed (e.g., femoral perineural infusion-induced quadriceps femoris weakness limiting ambulation, or an insensate extremity during infraclavicular or popliteal sciatic infusion). Of note, data derived from laboratory animals suggest that both ropivacaine and bupivacaine induce tissue injury,^{135,136} but ropivacaine results in significantly less damage.^{137,138} The clinical implications of these data remain unknown.

It also remains unknown whether the primary determinant of CPNB effects is solely local anesthetic dose (mass),^{129,131,139,140} or if volume (rate) and/or concentration exert additional influence. For single-injection nerve blocks, volume and concentration primarily determine efficacy when dose is held constant.^{141,142} However, for continuous blocks, data from the only study that varied both the infusion rate and concentration in a static ratio so that the total dose was comparable in each treatment group suggest that local anesthetic concentration does not influence block effects as long as the total dose remains constant.¹⁴³ Unfortunately, the results from this study of posterior lumbar plexus ropivacaine infusion may not be applicable to other anatomic locations,^{140,144–146} local anesthetics,^{127,132–134} infusion rates,^{67,140,147} local anesthetic concentrations,^{133,140,148–150} or bolus dose/volume combinations,¹⁴⁷ and thus further investigation is required for a definitive answer.

To complicate the issue, in the clinical setting, patient-controlled bolus doses and/or an adjustable basal infusion rate are often provided, and therefore total local anesthetic dose varies depending on individual patient requirements.^{57,129,144–146,151,152} In these clinical cases, it seems that concentration and rate do influence infusion effects.^{145,146,151} Unfortunately, currently published studies provide widely conflicting data, probably because of the many variables influencing infusion effects and analgesic requirements.^{129,144–146,151–153} For example, studies involving interscalene ropivacaine infusion report increasing local anesthetic concentration results in increased,¹²⁹ decreased,¹⁴⁴ or no^{152,153} difference in postoperative analgesia. Similarly, increasing local anesthetic concentration has differing effects on the incidence of an insensate extremity depending on catheter site location: increased for infraclavicular,¹⁴⁵ decreased for popliteal,¹⁴⁶ no difference for axillary,¹⁵³ and variable for interscalene.^{139,144,152} Therefore, no optimal concentration/rate combination may be recommended for all anatomic locations, and further study is warranted. For bupivacaine/levobupivacaine and ropivacaine, the most frequently cited concentrations are between 0.1% to 0.125% and 0.1% to 0.2%, respectively.

Several medications are occasionally added to the local anesthetic during CPNB in an attempt to improve analgesia without increasing motor block. There are reports of the inclusion of opioid with perineural local anesthetic,^{147,154,155} but currently there are insufficient data to draw any conclusions regarding its efficacy.^{156,157} Although clonidine was often added in the earlier years of CPNB,^{147,154,158–161} 3 subsequent RCTs failed to demonstrate any clinically relevant benefits.^{65,162,163} An additional RCT found no benefit to adding epinephrine to perineural ropivacaine,¹⁶⁴ and possible prolonged vasoconstriction places the safety of this practice into doubt.^{8,165–167} Additional possible adjuvants

have been reported, but none is currently approved for perineural use in patients,^{168,169} and some may have unacceptable systemic effects.¹⁶⁹

LOCAL ANESTHETIC DELIVERY REGIMENS

Infusates may be administered with 3 main strategies: exclusively as a basal infusion or bolus dose, and a combination of these 2 modalities. Unfortunately, similar to the data involving local anesthetic concentration, studies of delivery strategy are somewhat mixed (Table 2).^{170,171} In general, RCTs involving femoral and fascia iliaca infusions have reported few differences in analgesia among the various delivery regimens (other than reduced local anesthetic use with bolus-only dosing).^{154,158,172} Conversely, for sciatic catheters, providing a basal infusion maximizes analgesia and other benefits,^{170,171} although the data regarding the benefits of adding patient-controlled bolus doses are less clear.^{170,171,173}

Interestingly, providing automated, hourly, 5-mL bolus doses of levobupivacaine via a popliteal sciatic catheter decreased pain scores compared with patients receiving a continuous, 5-mL basal infusion of 0.125% levobupivacaine¹⁷⁴ (although a similar investigation involving femoral ropivacaine infusion failed to detect differences in sensory or motor effects).⁹⁴ However, by adding patient-controlled bolus doses to these 2 regimens, the difference in pain scores disappeared.¹⁷⁵ Importantly, all investigations report less total consumption of local anesthetic with regimens providing patient-controlled bolus doses, suggesting the desirability of including this modality for 3 main reasons: (1) decreasing the required basal infusion rate and thus theoretically decreasing motor block (inadequately investigated to date)^{94,133,176}; (2) decreasing the incidence of an insensate extremity³¹; and (3) increasing the duration of infusion/analgesia for ambulatory patients discharged with a finite volume of local anesthetic.^{170,177}

In contrast to the lower extremity, investigations of interscalene¹⁴⁷ and infraclavicular⁵⁷ perineural infusion are more uniform and suggest that including a basal infusion improves baseline analgesia, decreases the incidence and severity of breakthrough pain, and decreases sleep disturbances and supplemental analgesic requirements. Furthermore, adding patient-controlled bolus doses to a basal infusion decreases total local anesthetic consumption and supplemental analgesic requirements,^{57,147,173} allows block reinforcement during dressing changes or physical therapy,^{147,178,179} and may provide increased independent activity.¹⁷³ Additional RCTs attempting to further refine interscalene dosing report somewhat conflicting results. One study provides evidence that a high basal rate combined with low-volume, patient-controlled bolus doses reduces baseline pain scores and sleep disturbances, and decreases the incidence and severity of breakthrough pain, but at a cost of increasing local anesthetic consumption.⁶⁷ However, other similar investigations report few differences in varying the basal infusion rate.^{140,173,180}

Unfortunately, because of the heterogeneity of catheter types, insertion techniques, and a myriad of additional factors, there is little evidence for an “optimal” infusion regimen. Until recommendations based on prospectively collected data are available, health care providers may wish

Table 2. Local Anesthetic Delivery Regimens for Continuous Peripheral Nerve Blocks

Catheter location	Treatment groups				Primary findings
	n	Basal (mL/h)	Bolus (mL)	Lockout (min)	
Interscalene ¹⁴⁷					
• Nonstimulating catheter	20	10	—	—	Improved analgesia versus bolus only
• Anterolateral approach	20	5	2.5	30	Improved analgesia versus bolus only
• Sufentanil (0.1 µg/mL)	20	—	5	30	Increased supplemental analgesics versus other 2 groups
• Ropivacaine (0.2%)					
Interscalene ¹⁸⁰	38	2	5	60	Note that this group self-administered 6 mandatory bolus doses daily in addition to as-needed bolus doses
• Nonstimulating catheter	43	5	5	60	Increased incidence of an insensate hand, but no significant differences in pain, analgesics, awakenings
• Ultrasound-guided posterior approach					
Interscalene ⁶⁷	12	8	2	60	Increased baseline pain, breakthrough pain incidence and intensity, sleep disturbances, and dissatisfaction with analgesia
• Stimulating catheter	12	4	6	60	Increased consumption of local anesthetic with a shorter duration of infusion and analgesia
• Anterolateral approach					
Interscalene ¹⁷³	15	7	—	—	Possibly increased assistance with daily activity and time until 10 min of ambulation (data combined with popliteal infusion; no P value provided for ambulation)
• Nonstimulating catheter	15	5	2	12	Possibly lower incidence of "slight paresthesia" (data combined with popliteal infusion)
• Anterolateral approach	15	12	— ^a	—	Increased supplemental analgesics versus basal bolus
Infraclavicular ⁷⁷	15	8	4	60	Highest satisfaction scores versus other 2 groups
• Stimulating catheter	15	— ^a	9.9	60	Increased breakthrough pain incidence and intensity as well as sleep disturbances versus basal bolus
• Coracoid approach					
Axillary ⁵	10	10	—	—	No clinical differences between groups; but, study most likely underpowered to detect any difference
• Nonstimulating catheter	10	—	10	60	Note that this group received automated hourly bolus doses of 10 mL without additional optional bolus doses
Femoral ¹⁵⁴	15	10	—	—	Increased dynamic pain versus 5-mL bolus group and increased local anesthetic consumption versus others
• For hip arthroplasty	15	—	10	60	Highest satisfaction scores versus other 2 groups
• Inguinal perivascular approach					
• Nonstimulating catheter	15	—	5	30	Increased local anesthetic consumption versus other 2 groups
• inserted 10–15 cm using Seldinger technique	15	5	2.5	30	Trend toward less supplemental analgesic requirements (P = 0.10) than other 2 groups
Femoral ¹⁵⁸	15	—	10	60	
• For knee arthroplasty					
• Inguinal perivascular approach					
• Nonstimulating catheter					
• inserted 10–15 cm using Seldinger technique					

(Continued)

Table 2. (Continued)

Catheter location	Infusate(s)	Treatment groups			Primary findings
		n	Basal (mL/h)	Bolus (mL)	
Fascia iliaca ^{1,72}	Ropivacaine (0.2%)	46	10	—	Least local anesthetic consumption versus other 2 groups
• For knee surgery		46	5	5	
• Nonstimulating catheter inserted 10–15 cm without Seldinger technique		44	—	10	
Subgluteal sciatic ^{1,71}	Ropivacaine (0.2%)	25	10	—	Increased consumption of local anesthetic
• Nonstimulating catheter inserted 3–4 cm		25	5	5	
Popliteal sciatic ^{1,70}		10	12	— ^a	Increased consumption of local anesthetic with a shorter duration of infusion and analgesia
• Stimulating catheter		10	8	4	
• Posterior approach		10	— ^a	9.9	
Popliteal sciatic ^{1,74}	Levobupivacaine (0.125%)	22	5	—	Increased baseline and breakthrough pain intensity; a trend toward increased rescue analgesic requirement ($P = 0.055$) Note that this group received automated hourly bolus doses of 5 mL without additional optional bolus doses
• Nonstimulating catheter		22	—	5	
• Posterior approach		25	5	3	
Popliteal sciatic ^{1,75}	Levobupivacaine (0.125%)	25	—	5	Increased local anesthetic consumption Note that this group received automated hourly bolus doses of 5 mL; and optional 3-mL bolus doses
• Nonstimulating catheter		25	—	5	
• Posterior approach		25	—	3	
Popliteal sciatic ^{1,73}	Ropivacaine (0.2%)	15	7	—	Possibly increased assistance with daily activity and time until 10 min of ambulation (data combined with interscalene infusion; no P value provided for ambulation)
• Nonstimulating catheter		15	5	2	
• Posterior approach		15	5	2	Possibly lower incidence of “slight paresthesia” (data combined with interscalene infusion)

Due to publication limitations, includes only selected randomized, controlled trials specifically investigating varying local anesthetic delivery method.

— = not included for this treatment group.

^a Nominal basal infusion rate or bolus volume provided to retain treatment group masking.

to consider that most published investigations report a basal rate of 4 to 10 mL/h (lower rates for catheters of the lower extremity; higher rates for the upper extremity), a bolus volume of 2 to 10 mL, and a bolus lockout period of 20 to 60 minutes. Similarly, the maximum recommended hourly total dose of local anesthetic during perineural infusion remains unknown,¹⁸¹ but a wide safety margin has been documented in numerous clinical trials,^{125,140,148,182–187} with 1 study reporting no toxicity signs or symptoms with perineural ropivacaine 0.2% administered at basal rates up to 14 mL/h and large, repeated boluses of ropivacaine 0.5% (10–60 mL) provided for up to 27 days.¹⁸⁸

INFUSION PUMPS

Although perineural local anesthetic may be provided using exclusively human-administered bolus doses,¹⁸⁹ both clinical factors (e.g., basal infusion benefits) as well as logistical considerations¹⁹⁰ usually dictate the use of an infusion pump. There is no single optimal device for all situations, given the multitude of clinical scenarios and practice requirements, so pump preference is usually based on the desired device characteristics.¹⁹¹ Infusion pumps may be (arbitrarily) categorized by their power source. Although spring- and vacuum-powered devices are available, neither is particularly desirable for the purpose of CPNB because of a multitude of factors, including highly variable basal infusion rates and relatively small local anesthetic reservoir volumes, respectively.^{192,193} Until recently, elastomeric infusion pumps were severely limited relative to the capabilities of electronic devices¹⁹⁰; however, with the advent of newer nonelectronic pumps, this is no longer the case.

In general, electronic devices provide very accurate and consistent ($\pm 5\%$) basal infusion rates over the entire course of infusion.^{192–195} In contrast, elastomeric pumps usually overinfuse (110%–130% expected) during the initial 3 to 8 hours of infusion and within the final hours before reservoir exhaustion,^{192–196} resulting in a shorter infusion duration than anticipated given the initial reservoir volume and set basal infusion rate.^{192–195,197,198} However, whether the increased variability is clinically significant, or in which clinical situations it is relevant, remains unknown. Unlike electronic devices, the basal infusion rate of most elastomeric devices increases with increasing ambient temperature and pump height relative to the catheter insertion site,^{192–195,198} although these changes are probably clinically relevant only at extreme values.

An adjustable basal infusion rate allows local anesthetic administration titration in case of an insensate extremity,³¹ undesired side effects (e.g., muscle weakness),^{94,180} inadequate analgesia,¹⁷⁰ or desire to maximize infusion duration (e.g., ambulatory patients with a set reservoir volume).^{57,170,177} In addition, a patient-controlled bolus function often provides many clinical benefits.^{57,147} All electronic pumps provide an adjustable basal rate, patient-controlled bolus doses, and a variable bolus lockout period.^{192–195} Although most elastomeric devices provide a fixed basal infusion rate,¹⁹¹ a few now provide flexibility similar to their electronic counterparts. Nearly all electronic pumps use an external local anesthetic reservoir that allows for easy reservoir exchanges.^{116,188} In contrast, all elastomeric devices have an

internal reservoir. Even though refilling such devices has been investigated,^{199,200} this procedure is not approved by manufacturers/governments for the majority of devices, requiring the use of an additional unit if continued infusion is desired after reservoir exhaustion.^{173,201–203} Regardless of reservoir type, filling the infusion pump/reservoir within the United States must now be executed within an isolation class 5 environment, essentially requiring local anesthetic compounding within a designated pharmacy with a laminar flow workbench.²⁰⁴

Nonelectronic infusion pumps are often favored for their relative simplicity in both initially setting and subsequently adjusting the basal infusion rate²⁰⁵; for their light weight and smaller size²⁰⁶; their lack of audible alarms^{206,207} (although there is no warning for a pause in the infusion)²⁰⁸; disposability²⁰⁹; and for their silent operation (noise generated by electronic pumps may disturb patient sleep).²⁰⁶ In addition, elastomeric devices with a manufacturer-fixed basal rate and no bolus dose capability are usually relatively inexpensive.¹⁹¹ Conversely, reusable electronic pumps use inexpensive disposable “cassettes” to provide sterile infusion for individual patients.¹⁷⁷ A limited number of single-use electronic devices are available.^{144–146} Lastly, although the reliability for most infusion pumps is high, regardless of power source, certain devices are more dependable than others for both electronic^{207,210–213} and nonelectronic pumps.^{196,208}

AMBULATORY PERINEURAL INFUSION

First described in 1997,²¹⁴ CPNB may be provided to patients outside of the hospital using a portable infusion pump, and nearly every catheter type (i.e., anatomic location) has been reported in ambulatory patients.¹⁹¹ Perineural infusion is often provided for ambulatory surgery without an overnight hospital stay,^{84–86} but the technique may be used to shorten hospitalization^{178,215} and/or provide benefits after discharge either home or to a skilled nursing facility.^{33,200} Time constraints are often more restrictive in high-turnover ambulatory centers,⁸⁵ making insertion techniques with documented time savings frequently desirable (e.g., ultrasound guidance).^{61,64,105,216} Because patients are rarely directly monitored outside of the hospital, and not all patients desire or are capable of accepting the additional responsibility of caring for the catheter and pump system, patient selection criteria are often more stringent for ambulatory CPNB. In an effort to avoid local anesthetic toxicity, patients with renal or hepatic insufficiency are often excluded from outpatient perineural infusion.¹⁸² For infusions possibly affecting the phrenic nerve and weakening the ipsilateral diaphragm (e.g., interscalene and paravertebral catheters),^{217–219} caution is warranted for individuals with heart/lung disease and in obese patients who may not be able to compensate for mild hypoxia and/or hypercarbia.^{220,221} Of note, age alone is not an absolute exclusion criterion, with hundreds of pediatric patients receiving at-home CPNB without complication rates or severity higher than for their adult counterparts.^{14,24–26}

Providing ambulatory CPNB often leads to a reduced time until discharge readiness^{33,58,178,222} and, in some cases, actual discharge.^{178,215} After tricompartamental knee arthroplasty, permitting early discharge with ambulatory femoral

infusion results in decreased hospitalization-related costs.²²³ However, although ambulatory continuous femoral and posterior lumbar plexus nerve blocks decrease the time until important discharge criteria are met,^{33,58,222} an increased incidence of patient falls in patients receiving ropivacaine versus saline through their catheters suggests that increased caution is warranted before implementing early discharge.¹⁷⁶ Nevertheless, relatively small published series demonstrate the feasibility of total joint arthroplasty with only a single-night hospital stay, or even on an outpatient basis, when patients are permitted to continue their hospital-based perineural infusion at home.^{84,202,203,224,225}

Although the benefits of home CPNB are well documented with many placebo-controlled RCTs,^{31,33,34,58,93,178,222,226,227} there are negligible published data regarding the optimal practice for multiple aspects of ambulatory infusion, such as the requirement of a patient caretaker⁸⁶; method/frequency of patient oversight (e.g., home nursing visits,^{173,228,229} telephone calls,^{20,205} or simply written instructions with solely patient-initiated contact); and catheter removal protocol (health care provider extraction,^{173,229} caretaker withdrawal with instructions provided by telephone,²²² or simply written instructions²²⁶). Of 40 patients with a hospital-based CPNB, 13% stated they would be unwilling to remove their catheter at home.²³⁰ However, of patients who previously removed a perineural catheter at home, 98% felt "comfortable" doing the procedure with instructions given by telephone, only 4% would have preferred to return to the hospital for health care provider catheter removal, and 43% would have felt comfortable with exclusively written instructions.²⁰⁵ Of note, at least within the United States, there are no national guidelines regarding the maximal safe CPNB duration.²⁰⁴

BENEFITS OF CPNB

Whereas case reports and series suggest numerous possible benefits of CPNB for a wide variety of ailments,⁵⁻¹⁷ published RCTs include exclusively postoperative patients. Providing analgesia is the primary indication for postoperative CPNB,¹⁸ and most CPNB benefits seem to be dependent on successfully improving pain control (Table 3).¹⁸ Potent analgesia is most dramatic for surgical sites that are completely innervated by nerves affected by the perineural infusion, as is often the case for shoulder and foot procedures (interscalene and sciatic perineural catheters, respectively).^{31,34,93,178,215,226,230} Unfortunately, brachial plexus infusions for procedures at or distal to the elbow seem to provide less-impressive analgesia,²²⁷ even though they (theoretically) cover the entire surgical site. RCT-documented benefits of axillary,¹⁵³ supraclavicular,²³¹⁻²³³ and transversus abdominus plane²³⁴ infusion are severely lacking. Although the benefits of infraclavicular infusion are validated,²²⁷ analgesia is often less than optimal unless a high enough dose of local anesthetic is administered, frequently rendering the extremity insensate.^{57,145}

Similarly, femoral or posterior lumbar plexus infusion may result in unacceptable quadriceps femoris and hip adductor weakness when a high enough dose of local anesthetic is administered to optimize analgesia.⁹⁴ In addition, a single perineural infusion for surgical sites innervated by multiple nerves, most notably the hip, knee, and

ankle, may provide less than optimal analgesia without the concurrent use of additional analgesics.^{33,58,146} Of published reports, nearly all investigators provide a single infusion, often supplemented with a separate single-injection peripheral nerve block (e.g., sciatic block after knee surgery).²³⁵ Some individuals have proposed inserting a second catheter,²³⁶⁻²³⁸ although there are minimal and somewhat conflicting data to guide clinical practice.^{239,240} Whereas a lumbar epidural provides generally equivalent analgesia to femoral perineural infusion for hip and knee arthroplasty, CPNB results in a more favorable side-effect profile without the risk of epidural hematoma during concomitant anticoagulant administration.^{159,161,241,242}

Although the evidence for CPNB benefits during local anesthetic infusion is overwhelming, there are few data demonstrating benefits after catheter removal. Exceptions include improved analgesia after a few days^{2,32,243} or 6 months²⁴⁰; more rapid resumption of unassisted standing and lavatory use²; increased health-related quality of life in 1 study²⁴⁴ (but not 5 others)²⁴⁵⁻²⁴⁹; and faster tolerance of passive knee flexion² resulting in earlier discharge from rehabilitation centers.^{159,161} Conspicuously lacking is evidence of medium- or long-term improvements in health-related quality-of-life measures.²⁴⁵⁻²⁵⁰

COMPLICATIONS

As with all medical procedures, the potential CPNB benefits must be weighed against the potential risks. Fortunately, infusion-related serious and lasting injuries are uncommon, whereas relatively minor complications occur at a frequency similar to single-injection peripheral nerve blocks.²⁵¹ Unfortunately, heterogeneous catheter insertion techniques, equipment, anatomic locations, and infusions render generalizations difficult. For example, various prospective studies report an incidence of secondary block (infusion) failure of 1%,²⁵² 20%,³⁴ and 50%.³⁶ Thus, the specific complication rates provided in this section will not apply to all practices. CPNB-specific complications during catheter insertion include inaccurate catheter tip placement too far from the target nerve to provide postoperative analgesia,³⁵ and in exceptionally rare cases, epidural,²⁵³⁻²⁵⁵ intrathecal,²⁵⁶⁻²⁵⁸ intravascular,^{227,259} intraneural,²⁶⁰ and even interpleural catheter insertion.²⁶¹ Catheter migration after accurate placement has been suggested,²⁶² but also doubted,²⁶³ and the dearth of published events suggests that it is an exceptionally rare event, if it even occurs at all.

During the perineural infusion, more common (and benign) complications include catheter dislodgement or obstruction^{116,173,252} and fluid leakage at the catheter site.^{173,227} Although not prospectively investigated, subcutaneous catheter tunneling,^{41,264} application of liquid adhesive,¹⁹¹ use of a catheter anchoring device,¹⁹¹ and applying 2-octyl cyanoacrylate glue²⁶⁵ may decrease the incidence of dislodgement and leakage.

Additional possible complications include infusion pump malfunction,^{207,266} undesired pause,²⁰⁸ or disconnection³³; skin irritation or allergic reactions to the catheter dressing and/or liquid adhesive²⁶⁷; and catheter-induced brachial plexus irritation.²⁶⁸ In addition, a CPNB-induced insensate extremity may prove disconcerting to patients,²⁶⁹ impede

Table 3. Benefits of Continuous Peripheral Nerve Blocks Documented in Randomized Controlled Trials Including at Least One Treatment Group Without a Regional Anesthetic

Benefit	Brachial plexus			Femoral nerve			Sciatic nerve	
	Interscalene	Infracervical	Posterior lumbar plexus	Femoral	Fascia iliaca	Popliteal		
Analgesia (improved)	RCT ^{173,217,326-329,331,a} MPC ^{34,93,178}	MPC ²²⁷	RCT ^{113,238,346,b}	RCT ^{2,159,161,237,243,248,250,349,355,b} MPC ²²²	RCT ³⁵⁹	RCT ^{173,237,238,a,b} MPC ^{31,215,226}		
Resting	RCT ³²⁹	MPC ²²⁷		RCT ^{240,b}	RCT ³⁵⁹			
Breakthrough	MPC ^{34,93,178}							
Dynamic	RCT ^{173,329,331,a} MPC ¹⁷⁸		RCT ^{238,346,b}	RCT ^{2,159,161,237,240,243} MPC ^{32,b}		MPC ^{31,215,226} RCT ^{173,237,238,240,a,b}		
> 1 d after catheter removal				RCT ^{2,240,b} MPC ³²		RCT ^{240,b}		
Supplemental analgesic requirements (decreased)	MPC ^{34,93,178}	MPC ²²⁷		RCT ²⁴³ MPC ³²		MPC ^{31,215}		
Oral opioids	RCT ^{328,331} MPC ^{178,230}		RCT ^{346,348} MPC ³⁵²	RCT ^{2,36,150,167,240,243,244,250,346,349,355,b}	RCT ³⁵⁹	RCT ^{240,b} MPC ²¹⁵ RCT ^{173,a}		
IV opioids	RCT ^{173,217,326,327,331,a} MPC ³⁴	MPC ²²⁷	RCT ^{346,348}	RCT ^{161,242,248,346,356}		RCT ^{173,a} MPC ^{31,215}		
NSAID	RCT ^{173,326,327,a}		RCT ³⁴⁶	RCT ³⁴⁶		RCT ^{173,a} MPC ³¹		
Other	RCT ^{173,a} MPC ³⁴	MPC ²²⁷		RCT ^{237,248,b}	MPC ³⁵⁸	RCT ^{173,237,a,b} MPC ³¹		
Opioid-related side effects (decreased)								
Nausea, vomiting, or antiemetic rescue								
Pruritus								
Sedation, fatigue, dizziness, or bowel function								
Sleep								
Sleep disturbance	RCT ^{173,a}	MPC ²²⁷				RCT ^{173,a} MPC ^{31,226}		
Awakenings	MPC ^{34,93}	MPC ²²⁷				MPC ³¹		
Satisfaction	RCT ^{173,217,327,328,a} MPC ^{34,93,178}	MPC ²²⁷	RCT ^{346,348} MPC ³³	RCT ^{248,250,346}	RCT ³⁵⁹	RCT ^{173,a} MPC ^{31,215}		
Discharge (decreased time until ...)								
Discharge readiness	MPC ¹⁷⁸		MPC ³³	MPC ^{58,222}		RCT ^{173,a} MPC ²¹⁵		
Actual discharge	RCT ^{173,a} MPC ¹⁷⁸			RCT ^{159,161}				
Resumption of passive joint range of motion (accelerated)								
Shoulder	MPC ¹⁷⁸							
Knee								
Hip								
Resumption of ambulation or other functioning (accelerated)	RCT ^{173,a}		RCT ³⁴⁶ MPC ³⁵² RCT ^{238,b}	RCT ^{2,36,159,161,237,248}	RCT ³⁵⁹	RCT ^{237,b}		
Inflammation or proinflammatory markers (decrease)								

Only selected references are included because of publication limitations.

RCT = randomized controlled trial (either no placebo control or at least 1 clinical group unmasked to treatment allocation); MPC = RCT with all clinical groups masked to treatment allocation and including a placebo control; NSAID = nonsteroidal antiinflammatory drug.

^a The study by Capdevila et al.¹⁷³ did not separate results for interscalene and popliteal sciatic catheters, and therefore one or both of these anatomic locations may account for all of the difference between treatment groups.

^b Studies by Bagy et al.,²³⁸ Mistraretti et al.,²³⁷ and Blumenthal et al.²⁴⁰ compared 2 concurrent continuous peripheral nerve blocks versus no regional intervention, and therefore one or both of these anatomic catheter locations may account for all of the difference between treatment groups.

physical therapy and/or ambulation,^{133,222} and be considered a risk factor for injury by some investigators.^{145,146} In these cases, the infusion pump is usually paused until sensory perception begins to return, after which the infusion is restarted at a lower basal rate.^{31,58} Conversely, inadequate analgesia or breakthrough pain may occur, and is often treated by increasing the basal infusion and providing patient-controlled bolus doses, respectively.^{31,227}

More serious (but very rare) complications include myonecrosis with repeated large boluses of bupivacaine²⁷⁰; systemic local anesthetic toxicity^{126,148,182,271,272}; prolonged Horner syndrome²⁷³; and catheter knotting,^{75,76,274} retention,^{57,275} shearing,^{126,276,277} or breakage.²⁷⁸ Although infusions potentially affecting the phrenic nerve may have minimal pulmonary effects for relatively healthy patients,^{155,217,279} dyspnea is somewhat common,⁶⁷ and lower lobe collapse has occurred.²²¹ There is limited evidence that the risk of nerve injury from prolonged local anesthetic exposure may be increased in patients with diabetes^{280,281} and/or preexisting neuropathy.²⁸²

There are case reports of peri-catheter hematoma formation,^{276,283} often with concurrently administered low-molecular-weight heparin for thromboprophylaxis.^{284–286} Most are self-limiting,²⁸⁵ but more dramatic cases require surgical evacuation.²⁸³ The most recent (Third) American Society of Regional Anesthesia consensus statement on neuraxial anesthesia and anticoagulation explicitly recommends precautions for neuraxial techniques and that anticoagulation be exercised for “deep” perineural catheters (undefined); specifically, that any catheter be removed before administration of various anticoagulants,²⁸⁷ although this practice has been questioned by various investigators.^{288–293} Also concerning is the association between perineural infusions affecting the femoral nerve and patient falls after hip and knee arthroplasty,¹⁷⁶ possibly because of CPNB-induced sensory, proprioception, and/or quadriceps weakness.⁹⁴ Correlation does not prove causation; however, until further evidence is published, practitioners should consider interventions that may decrease the risk of falls, such as limiting the local anesthetic dose/mass¹⁴³; providing crutches/walker and a knee immobilizer during ambulation²⁹⁴; and educating surgeons, nurses, and physical therapists of possible CPNB-induced deficits and fall precautions.

Although the reported rates of inflammation (3%–4%)^{252,266,295} and catheter bacterial colonization (6%–57%) are seemingly high,^{296,297} clinically relevant infection is relatively rare (incidence 0%–3%)^{298,299}; but most reports (<1%).^{38,126,251,296,300} Risk factors include admission to an intensive care unit, absence of perioperative antibiotic prophylaxis, and male sex.²⁶⁶ Although 1 multicenter study found a higher risk with axillary and femoral catheters,²⁶⁶ others have reported the interscalene location as the most problematic.^{252,299} Risk of infection is also correlated with infusion duration.²⁶⁶ Nonetheless, infusions provided during extended medical transport for up to 34 days¹¹⁶ and provided at home for up to 83 days²⁰⁰ have been reported with a minimal incidence of infection. There is limited evidence that subcutaneous catheter tunneling²⁶⁴ may decrease the risk of bacterial colonization and infection.²⁹⁶ Abscesses have occurred, although the incidence remains

unknown, and occasionally require surgical treatment,³⁰¹ but often do not if timely antibiotic coverage is provided.^{302–304} Although life-threatening catheter-related infections/sepsis have been reported,^{305,306} there is currently no case of permanent injury due to CPNB-related infection within the English-language literature.²⁹⁸

Perhaps the most feared postinfusion complication is neurologic injury.³⁰⁷ It is often difficult to determine how much of a neurologic deficit, if any, is attributable to CPNB because all surgical procedures are associated with a variable incidence of nerve injury,³⁰⁸ regardless of the application of a regional anesthetic/analgesic.^{309,310} For example, hip arthroplasty without a regional anesthetic is associated with an incidence of femoral neuropathy as high as 2.3%.³¹⁰ So, if a study with a regional anesthetic/analgesic in this same patient population found a 1% incidence of femoral neuropathy, it would suggest that the perineural infusion is actually protective; but such an uncontrolled study would seem alarming with such a high incidence of nerve injury “associated” with CPNB. With this critical limitation in mind, the incidence of transient adverse neurologic symptoms associated with CPNB is 0% to 1.4% for interscalene,^{38,251,252,266,276} 0.4% to 0.5% for femoral,^{266,276} and 0% to 1.0% for sciatic catheters.^{252,266,272,276} An additional investigation found a 0.2% incidence of neurologic deficits lasting longer than 6 weeks in nearly 3500 catheters from multiple anatomic locations.²⁵² In this latter study, it remains unknown whether the deficits resolved after the 6-week study period, but multiple prospective investigations report that the overwhelming majority of neurologic symptoms present at 4 to 6 weeks resolve spontaneously within 3 months of surgery.^{38,251,266}

There are reported cases of long-term and/or permanent nerve injury in patients with perineural infusion.³¹¹ Five large, prospective series^{38,251,266,272,276} that followed patients for at least 3 months found 3 cases of unresolved adverse neurologic events: a brachial plexus lesion after interscalene infusion (followed 9 months)²⁵¹; a femoral neuropathy presumably the result of a retroperitoneal hematoma (cause undetermined; months followed not reported)²⁷⁶; and a persistent paraesthesia after a popliteal sciatic catheter (followed through 18 months).²⁷² Combining the results of these studies (4148 subjects) suggests that the risk of neurologic injury lasting longer than 9 months associated with CPNB is 0.07%.^{38,251,266,272,276} It remains unknown whether CPNB contributed to these cases, or if they would have occurred without the addition of a regional analgesic. Although ultrasound guidance may decrease the incidence of many/most of these reported complications,³¹² there are few data supporting this proposition,^{313,314} and case reports suggest that completely abolishing such events is unlikely (quite possibly because postoperative neuropathy may occur without any regional anesthetic/analgesic).^{315–317}

CONCLUSIONS

Although the published literature presented in this review article provides a plethora of information involving CPNB, many aspects of perineural infusion have yet to be fully elucidated, including the optimal catheter insertion modality and technique; infusate(s) and adjuvants; local anesthetic delivery regimen; details of optimizing ambulatory

infusion; possible infusion benefits; and the incidence of all possible risks. Furthermore, although CPNB seems to provide far more potent analgesia than wound catheters,^{318–320} and often fewer undesirable side effects than epidural infusion,^{23,159,161,242,318} many questions remain regarding the optimal analgesic technique for many surgical procedures.^{321,322} Lastly, perineural infusion must be adequately compared with possible new analgesic techniques.^{244,323} Only through prospective research will we fully reveal and maximize the potential benefits, while minimizing the potential risks, of CPNB for our patients. ■

DISCLOSURES

Name: Brian M. Ilfeld, MD, MS.

Contribution: This author helped design the study, conduct the study, and write the manuscript.

Attestation: Brian M. Ilfeld approved the final manuscript.

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FAER'S IMPACT ON MY CAREER

Brian M. Ilfeld, MD, MS (Clinical Investigation).

Two years after completing my regional anesthesia fellowship, I was awarded a Foundation for Anesthesia Education and Research (FAER) Mentored Research Training Grant. This funding provided the opportunity to earn a Master's Degree in Clinical Investigation, as well as allowing completion of multiple pilot studies involving my primary interest at the time, ambulatory continuous peripheral nerve blocks. These exploratory investigations provided data included in a grant proposal sent to the National Institutes of Health (NIH), which was ultimately funded as a 5-year Mentored Career Development Award (in large part because of the Master's Degree the FAER award enabled). The NIH grant provided funding for 80% nonclinical time in addition to specific randomized controlled trials (also involving ambulatory perineural local anesthetic infusion). Five years of protected research time allowed me to take a dozen additional didactic courses to build on knowledge gained during my Master's Degree training; develop skills in designing, executing, and reporting multicenter clinical trials; work with and learn from incredibly talented coinvestigators; serve as an editor for my subspecialty's journal *Regional Anesthesia and Pain Medicine*; successfully compete for additional research funding; and help mentor wonderfully gifted and enthusiastic fellows and faculty members with whom I have been so blessed to cross paths. Most importantly, it gave me the opportunity to work and/or study with extraordinary mentors such as Drs. Kayser Enneking, Nikolaus Gravenstein, Daniel Sessler, Joseph Neal, James Eisenach, Tony Yaksh, and Pamela Duncan, among so many others. Now, 90% of my workweek involves clinical research, and I am very fortunate to serve as the Director of Clinical Research for my

section at the University of California San Diego, on the Advisory Board of the UCSD Clinical and Translational Research Institute, and as a reviewer for NIH Special Emphasis Panel/Scientific Review Groups. There is no doubt in my mind that without the investment FAER made in me nearly a decade ago, I would have been able to attain only a small fraction of my career goals. For this, I am, and will for always be, deeply grateful.

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Tripping Over Perineural Catheters

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Continuous peripheral nerve blockade (CPNB) is a technique that promises much, delivers plenty, and may yet be capable of more. Attractive to patients and clinicians alike for its ability to prolong the duration of analgesia, and to allow individualized dosing to be tailored to need, the uses of CPNB extend beyond the confines of hospitals to the continuation of high-quality analgesia in the ambulatory setting. Postoperative benefits of CPNB include reduced use of opioids (and consequently reduced side effects),^{1–3} reduced pain on movement,^{1,4} and improved quality of sleep.⁵ Numerous other indications have been described, including the retrieval of trauma patients, and the induction of sympathectomy to improve peripheral perfusion.³ Technical advancements in equipment and nerve localization, combined with a range of local anesthetic drugs and delivery systems, provide the anesthesiologist with what may seem a dizzying array of variables in the practical application of this technique. In this issue of *Anesthesia & Analgesia*, Brian Ilfeld, himself a major contributor to evidence in the field of CPNB, reviews a very large and heterogeneous body of work relating to the applications of CPNB in modern anesthetic practice.³ The result is a comprehensive summary and insightful interpretation of the literature to date, as well as the exposure of many significant voids that still remain regarding the optimal use and delivery of this important treatment modality.

The postoperative aims of CPNB are intimately related to the surgical procedure concerned, whether or not a period of intense pain is expected (and for how long), and how motor blockade may impact upon the rehabilitation phase. A case in point is the use of continuous femoral nerve block (CFNB) following total knee arthroplasty (TKA), a surgical procedure often associated with severe pain, whose site is innervated by more than one major peripheral nerve, and which requires a period of intense postoperative physical therapy and rehabilitation. This is

one of the most extensively researched applications of CPNB, with over 30 of the articles referred to in the accompanying review relating to CFNB in the setting of TKA.³ However, CFNB has been associated with quadriiceps weakness,^{6,7} which may impair active participation in physical therapy, and has been implicated in falls.⁸ In fact, dense motor block to reduce muscle spasm was the postoperative goal for successful CFNB in one of the landmark studies designed to investigate the use of CFNB following TKA.⁴ This outdated paradigm included prolonged admissions in rehabilitation centers and involved passive motion rehabilitation techniques, as did another influential study of CFNB.⁹ In the modern-day reality of accelerated clinical pathways, the seemingly competing goals of analgesia and mobility surrounding TKA therefore merit thoughtful consideration and further evaluation. Furthermore, the ideal local anesthetic regime for CPNB must be defined by clinically meaningful outcomes for contemporary practice, especially pain and mobility during hospitalization and functional recovery in the longer term.

Delving more deeply into the objectives of CPNB therefore generates more questions. How may sensory and motor block be optimally balanced and how may this balance change at different anatomical sites? Whereas the combination of opioids and low-concentration local anesthetics in epidural infusions can produce effective analgesia with minimal motor block,^{10,11} there are limited data for how volume, concentration, and total mass of local anesthetic influence motor and sensory blocks in CPNB. It appears likely that the site of block may have a bearing on this, with anatomical differences in the spaces around nerves and topographical differences within the nerves themselves potentially playing a role in the relationship between concentration, volume, and clinical effects.^{12,13} Total drug dose appears to be the primary determinant of clinical effects in continuous lumbar plexus block,¹⁴ whereas profound sensory block appears more common in low-concentration, high-volume popliteal-sciatic block,¹² and mixed results have been presented for continuous interscalene block.³ There are limited data on the optimal dose and concentration for CFNB following TKA, with most investigations focusing on the analgesic effects of changing concentration^{2,15} and scant evidence regarding the effects of concentration on motor block and mobility.¹⁶ Ilfeld and colleagues recently attempted to quantify the effects of a 4-day CFNB infusion, in comparison with a CFNB infusion stopped the morning after surgery, on readiness to hospital discharge following TKA, according

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to 3 explicit criteria relating to both mobility and analgesia.^{6,17} In 2 studies of near-identical methodology, but different settings (research center versus general orthopedic ward), the time to readiness to discharge in the 4-day CFNB group was significantly shorter, although the effect was less marked in the general orthopedic ward setting. Because all patients were ASA physical status II, and preoperative daily opioid use was an exclusion criterion, it is uncertain whether these results are generalizable to the wider TKA population. It is also noteworthy that although the mode of local anesthetic administration, patient-controlled bolus dosing instead of continuous rate infusion, can reduce the total consumption of local anesthetic without compromising analgesia,^{18–20} there is insufficient evidence to support any relative preservation of motor function.

In his review, Ilfeld addresses the evidence for alternatives to CPNB, and duly calls for further research.³ By targeting nerves more peripherally, CPNB could be used to more elegantly achieve analgesia with fewer troubling motor effects. One interesting and promising trial of continuous blockade of the obturator and saphenous nerves (adductor canal block) has reported pain scores and morphine consumption following TKA comparable to studies using femoral nerve block.²¹ Adductor canal block should theoretically have minimal motor effects; unfortunately, quadriceps strength was not an outcome measured in this preliminary study.

There is also a growing body of evidence around local infiltration analgesia (LIA) during and after major joint arthroplasty. The simplicity and apparent safety of this approach to analgesia, combined with an avoidance of the motor block associated with CPNB, make it particularly appealing as an alternative strategy. A recent review of the evidence on LIA for hip and knee arthroplasty commented on a number of methodological issues complicating data interpretation, but concluded that there is evidence to recommend intraoperative LIA for TKA for an initial postoperative analgesic effect of around 6 to 12 hours.²² There have been few direct comparisons of CFNB and LIA and only 1 double-blind randomized comparison of these 2 techniques.²³ This study reported significantly less morphine use, and improved functional recovery at 6 weeks, in the CFNB group. In addition, there was no difference between groups in the secondary outcome of 2-minute walk tests on postoperative days 1 to 3. This is in contrast to a nonblinded comparison of CFNB with LIA, which reported lower pain scores, less morphine consumption, and a greater number of patients mobilizing more than 3 m on postoperative day 1 in the LIA group, although the CFNB local anesthetic infusion regimen was most unconventional.²⁴ Another recent comparison of LIA and CFNB following TKA found pain scores and morphine consumption to be similar in the first 24 postoperative hours, but was not blinded, and had less robust methodology for data collection than did the study by Carli and colleagues.^{23,25} It is clear that high-quality double-blind trials are needed to further evaluate the roles of CFNB and LIA in the context of TKA.

Finally and importantly, with the exception of the comparison of CFNB and LIA by Carli and colleagues,²³ most investigations of long-term outcomes suggest little impact of

extended CPNB on measures of function in the months and years following hip or knee arthroplasty.^{1,4,9,26–31}

Where then do catheters belong in modern practice? The potential applications are many, the variables in practice are myriad, but the aims of adequate analgesia combined with early mobilization, rapid hospital discharge, and the best possible long-term outcomes present a challenge not yet fully answered. ■■

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Tripping Over Perineural Catheters

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Continuous peripheral nerve blockade (CPNB) is a technique that promises much, delivers plenty, and may yet be capable of more. Attractive to patients and clinicians alike for its ability to prolong the duration of analgesia, and to allow individualized dosing to be tailored to need, the uses of CPNB extend beyond the confines of hospitals to the continuation of high-quality analgesia in the ambulatory setting. Postoperative benefits of CPNB include reduced use of opioids (and consequently reduced side effects),¹⁻³ reduced pain on movement,^{1,4} and improved quality of sleep.⁵ Numerous other indications have been described, including the retrieval of trauma patients, and the induction of sympathectomy to improve peripheral perfusion.³ Technical advancements in equipment and nerve localization, combined with a range of local anesthetic drugs and delivery systems, provide the anesthesiologist with what may seem a dizzying array of variables in the practical application of this technique. In this issue of *Anesthesia & Analgesia*, Brian Ilfeld, himself a major contributor to evidence in the field of CPNB, reviews a very large and heterogeneous body of work relating to the applications of CPNB in modern anesthetic practice.³ The result is a comprehensive summary and insightful interpretation of the literature to date, as well as the exposure of many significant voids that still remain regarding the optimal use and delivery of this important treatment modality.

The postoperative aims of CPNB are intimately related to the surgical procedure concerned, whether or not a period of intense pain is expected (and for how long), and how motor blockade may impact upon the rehabilitation phase. A case in point is the use of continuous femoral nerve block (CFNB) following total knee arthroplasty (TKA), a surgical procedure often associated with severe pain, whose site is innervated by more than one major peripheral nerve, and which requires a period of intense postoperative physical therapy and rehabilitation. This is

one of the most extensively researched applications of CPNB, with over 30 of the articles referred to in the accompanying review relating to CFNB in the setting of TKA.³ However, CFNB has been associated with quadriiceps weakness,^{6,7} which may impair active participation in physical therapy, and has been implicated in falls.⁸ In fact, dense motor block to reduce muscle spasm was the postoperative goal for successful CFNB in one of the landmark studies designed to investigate the use of CFNB following TKA.⁴ This outdated paradigm included prolonged admissions in rehabilitation centers and involved passive motion rehabilitation techniques, as did another influential study of CFNB.⁹ In the modern-day reality of accelerated clinical pathways, the seemingly competing goals of analgesia and mobility surrounding TKA therefore merit thoughtful consideration and further evaluation. Furthermore, the ideal local anesthetic regime for CPNB must be defined by clinically meaningful outcomes for contemporary practice, especially pain and mobility during hospitalization and functional recovery in the longer term.

Delving more deeply into the objectives of CPNB therefore generates more questions. How may sensory and motor block be optimally balanced and how may this balance change at different anatomical sites? Whereas the combination of opioids and low-concentration local anesthetics in epidural infusions can produce effective analgesia with minimal motor block,^{10,11} there are limited data for how volume, concentration, and total mass of local anesthetic influence motor and sensory blocks in CPNB. It appears likely that the site of block may have a bearing on this, with anatomical differences in the spaces around nerves and topographical differences within the nerves themselves potentially playing a role in the relationship between concentration, volume, and clinical effects.^{12,13} Total drug dose appears to be the primary determinant of clinical effects in continuous lumbar plexus block,¹⁴ whereas profound sensory block appears more common in low-concentration, high-volume popliteal-sciatic block,¹² and mixed results have been presented for continuous interscalene block.³ There are limited data on the optimal dose and concentration for CFNB following TKA, with most investigations focusing on the analgesic effects of changing concentration^{2,15} and scant evidence regarding the effects of concentration on motor block and mobility.¹⁶ Ilfeld and colleagues recently attempted to quantify the effects of a 4-day CFNB infusion, in comparison with a CFNB infusion stopped the morning after surgery, on readiness to hospital discharge following TKA, according

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to 3 explicit criteria relating to both mobility and analgesia.^{6,17} In 2 studies of near-identical methodology, but different settings (research center versus general orthopedic ward), the time to readiness to discharge in the 4-day CFNB group was significantly shorter, although the effect was less marked in the general orthopedic ward setting. Because all patients were ASA physical status II, and preoperative daily opioid use was an exclusion criterion, it is uncertain whether these results are generalizable to the wider TKA population. It is also noteworthy that although the mode of local anesthetic administration, patient-controlled bolus dosing instead of continuous rate infusion, can reduce the total consumption of local anesthetic without compromising analgesia,^{18–20} there is insufficient evidence to support any relative preservation of motor function.

In his review, Ilfeld addresses the evidence for alternatives to CPNB, and duly calls for further research.³ By targeting nerves more peripherally, CPNB could be used to more elegantly achieve analgesia with fewer troubling motor effects. One interesting and promising trial of continuous blockade of the obturator and saphenous nerves (adductor canal block) has reported pain scores and morphine consumption following TKA comparable to studies using femoral nerve block.²¹ Adductor canal block should theoretically have minimal motor effects; unfortunately, quadriceps strength was not an outcome measured in this preliminary study.

There is also a growing body of evidence around local infiltration analgesia (LIA) during and after major joint arthroplasty. The simplicity and apparent safety of this approach to analgesia, combined with an avoidance of the motor block associated with CPNB, make it particularly appealing as an alternative strategy. A recent review of the evidence on LIA for hip and knee arthroplasty commented on a number of methodological issues complicating data interpretation, but concluded that there is evidence to recommend intraoperative LIA for TKA for an initial postoperative analgesic effect of around 6 to 12 hours.²² There have been few direct comparisons of CFNB and LIA and only 1 double-blind randomized comparison of these 2 techniques.²³ This study reported significantly less morphine use, and improved functional recovery at 6 weeks, in the CFNB group. In addition, there was no difference between groups in the secondary outcome of 2-minute walk tests on postoperative days 1 to 3. This is in contrast to a nonblinded comparison of CFNB with LIA, which reported lower pain scores, less morphine consumption, and a greater number of patients mobilizing more than 3 m on postoperative day 1 in the LIA group, although the CFNB local anesthetic infusion regimen was most unconventional.²⁴ Another recent comparison of LIA and CFNB following TKA found pain scores and morphine consumption to be similar in the first 24 postoperative hours, but was not blinded, and had less robust methodology for data collection than did the study by Carli and colleagues.^{23,25} It is clear that high-quality double-blind trials are needed to further evaluate the roles of CFNB and LIA in the context of TKA.

Finally and importantly, with the exception of the comparison of CFNB and LIA by Carli and colleagues,²³ most investigations of long-term outcomes suggest little impact of

extended CPNB on measures of function in the months and years following hip or knee arthroplasty.^{1,4,9,26–31}

Where then do catheters belong in modern practice? The potential applications are many, the variables in practice are myriad, but the aims of adequate analgesia combined with early mobilization, rapid hospital discharge, and the best possible long-term outcomes present a challenge not yet fully answered. ■■

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