Brachial Plexus Anesthesia: Essentials Of Our Current Understanding

Joseph M. Neal, M.D., James R. Hebl, M.D., J. C. Gerancher, M.D., and Quinn H. Hogan, M.D.

Brachial plexus regional anesthesia has been a mainstay of the anesthesiologist's armamentarium since Hall[1] first reported the use of cocaine to block upper extremity nerves in 1884. The American Society of Regional Anesthesia and Pain Medicine (ASRA) has sponsored a unique educational endeavor to provide practitioners and academicians alike with a comprehensive resource pertaining to brachial plexus anesthesia. Initially presented as an all-inclusive workshop at its May 2001 meeting, the material is available in its entirety on the ASRA Web site (www.asra.com). This review is a summary that presents the essential scholarly work resulting from this effort. It strives to (1) serve as a review of pertinent brachial plexus anatomy, (2) compare the efficacy of brachial plexus approaches and techniques, (3) describe the complications inherent to brachial plexus anesthesia, and (4) present available evidence to guide selection of drugs. Because evidence-based data pertaining to brachial plexus anesthesia is incomplete, we acknowledge informational gaps and emphasize areas in which we believe further study is needed. Readers desiring a more in-depth discussion of specific topics will find it in the Web site source documents, which also include additional anatomic photographs.

From Virginia Mason Medical Center (J.M.N), Seattle, Washington; Mayo Clinic (J.R.H.), Rochester, Minnesota; Wake Forest University (J.C.G.), Winston-Salem, North Carolina; and Medical College of Wisconsin (Q.H.H.), Milwaukee, Wisconsin.

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Brachial Plexus Anatomy

Upper extremity regional anesthesia requires a thorough knowledge of brachial plexus anatomy to facilitate the technical aspects of block placement and optimize the patient-specific block selection. The brachial plexus (Fig 1) is defined as that network of nerves supplying the upper extremity and formed by the union of the ventral primary rami of cervical nerves 5 through 8 (C5-C8), including a greater part of the first thoracic nerve (T1). Variable contributions may also come from the fourth cervical (C4) and second thoracic (T2) nerves.[2] The ventral rami are the roots of the brachial plexus and are variable in their mode of junction. The C5 and C6 rami unite near the medial border of the middle scalene muscle to form the superior trunk of the plexus, the C7 ramus becomes the middle trunk, and the C8 and T1 contributions unite to form the inferior trunk. The interscalene groove is defined as the palpable surface anatomy between the anterior and middle scalene muscles and allows clinicians easy and reliable access to the roots and trunks of the brachial plexus (Figs 2 and 3). The 3 trunks undergo primary anatomic separation into anterior (flexor) and posterior (extensor) divisions at the lateral border of the first rib. Divisions undergo yet another stage of reorganization into cords. The anterior divisions of the superior and middle trunks form the lateral cord of the plexus, the posterior divisions of all 3 trunks form the posterior cord, and the anterior division of the inferior trunk forms the medial cord. The 3 cords divide and give rise to the terminal branches of the plexus, with each cord possessing 2 major terminal branches and a variable number of minor intermediary branches.[2] The lateral cord contributes the musculocutaneous nerve and the lateral root of the median nerve. The posterior cord generally supplies the dorsal aspect of the upper extremity via the radial and axillary nerves. The medial cord contributes the ulnar nerve and the medial root of the median nerve. Important intermediary branches of the medial cord include the medial antebrachial cutaneous nerve of the

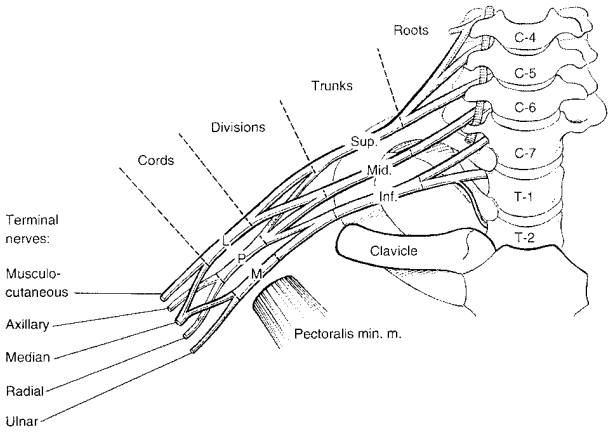

Fig 1. Brachial plexus anatomy. L, lateral; P, posterior; M, medial. (Reprinted with permission from Mayo Foundation.[50])

forearm and the medial cutaneous nerve of the arm, which joins with the intercostobrachial nerve (Fig 4) to innervate the skin over the ulnar aspect of the arm. Despite the aforementioned classic schema, anatomists have described 7 major configurations of the brachial plexus, with none having more than a 57% representation and 61% of bodies exhibiting right/left asymmetry.[3]

In addition to the neural plexus, several vascular structures have clinical importance as anatomic landmarks or structures to avoid. The vertebral artery travels cephalad and enters a bony canal formed by the transverse processes at the C6 level. As the cervical roots of the brachial plexus leave the transverse processes, they course immediately posterior to the vertebral artery,[4] which offers an interposed portal for potential intravascular injection.

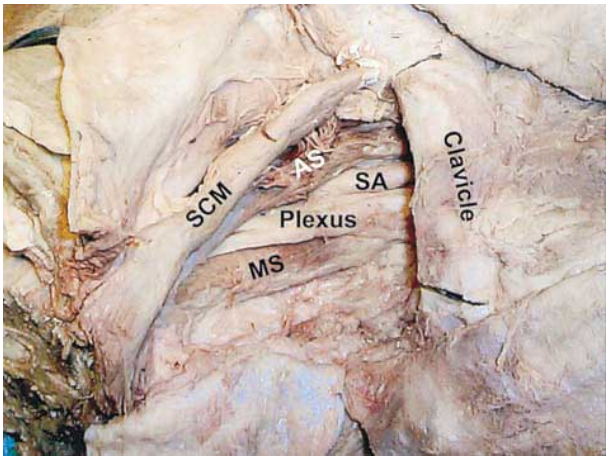

Fig 2. Right neck dissection. Head is left, anterior is up. SCM, sternocleidomastoid muscle; AS, anterior scalene muscle; SA, subclavian artery; MS, middle scalene muscle. The clavicle has been sectioned in 2 places.

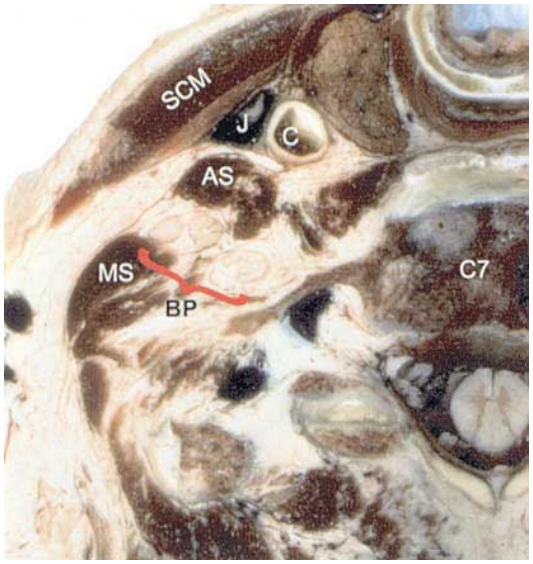

Fig 3. Cryomicrotome axial section of the left neck. Anterior is up. SCM, sternocleidomastoid muscle; J, jugular vein; C, carotid artery; AS, anterior scalene muscle; MS, middle scalene muscle; BP, brachial plexus; C7, 7th cervical vertebra.

The external jugular vein often overlies the interscalene groove at the level of C6 but is not a reliable or consistent anatomic marker. The subclavian artery is near the brachial plexus as they course over the first rib (Fig 2). Here the divisions of the brachial plexus lie posterior, cephalad, and lateral to the subclavian artery,[4] offering a consistent and valuable anatomic relationship during placement of supraclavicular blocks (Fig 5). The classic anatomic vascular relationship is defined by the axillary artery, which assumes its characteristic location in relation to the following terminal branches of the plexus: anterior to the radial nerve, posteromedial

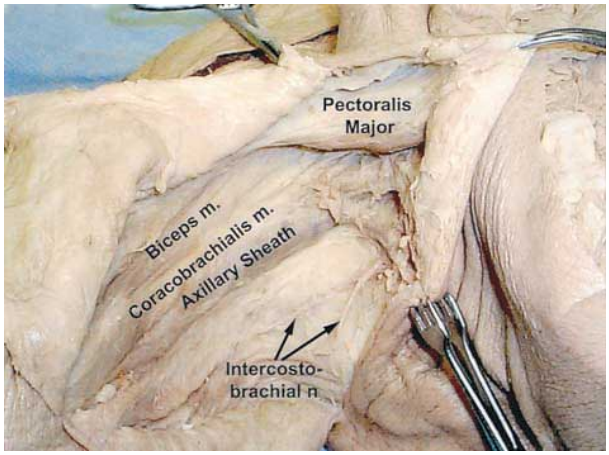

Fig 4. Right axillary dissection. The head is at the top of the image and the arm extends to the left of the image.

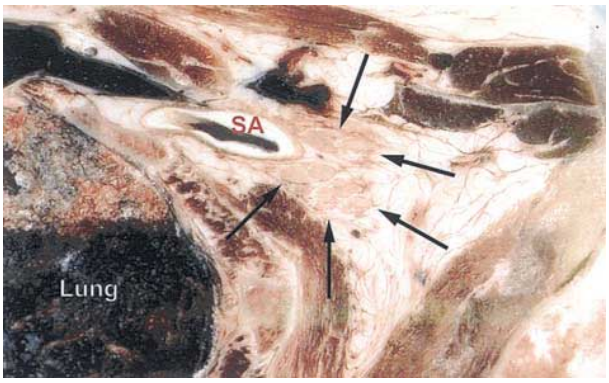

Fig 5. Cryomicrotome axial section, through the base of neck and apex of the axilla. Anterior is top. Arrows delineate components of the brachial plexus within thin layers interspersed with lobules of fat, such that no coherent sheath is evident. Note the posterior and lateral location of the plexus relative to the subclavian artery (SA).

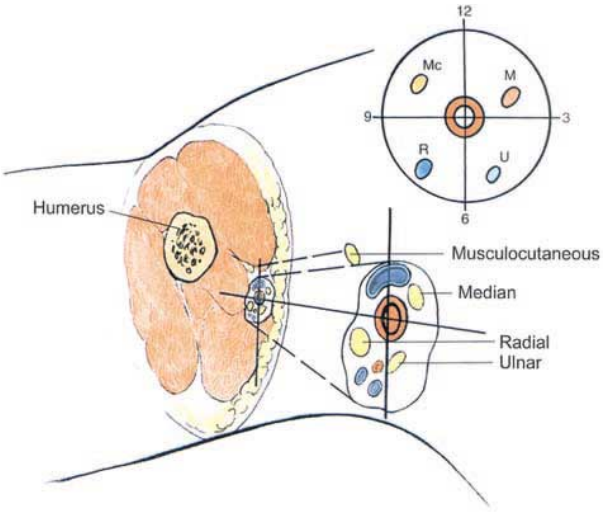

Fig 6. Typical anatomic relationship of the axillary artery to the terminal branches of the brachial plexus. Note that the musculocutaneous nerve has coursed away from the plexus at this level. (Reprinted with permission.[4])

to the median nerve, and posterolateral to the ulnar nerve (Fig 6). Vascular relationships are affected by changes in arm position and applied external pressure during regional block performance.

Axillary Sheath

The axillary sheath is a collection of connective tissue surrounding the neurovascular structures of the brachial plexus. It is a continuation of the prevertebral fascia separating the anterior and middle scalene muscles. Original descriptions of the sheath considered it to be a dense tubular structure extending from above the first rib to a point distal in the axilla.[5,6] It was believed that the axillary vessels and nerves were all lying loose within its center, implying that conduction anesthesia of the upper extremity could be performed with a single injection at any site along the sheath, with local anesthetic volume being the primary determinant for successful block. However, several investigators have since challenged the concept of a tubular axillary sheath,[7-9] proposing instead that the sheath is a multicompartmental structure formed by thin layers of fibrous tissue surrounding the plexus in filmy membranes[8] and extending inward to create discrete fascial septae (Figs 4 and 5). Nerves are thus enmeshed in this tissue rather than lying separate and distinct. As a result, individual fascial compartments are created for each nerve and define the anatomic limits for that neural structure. These compartments could functionally limit the circumferential spread of injected solutions, thereby requiring separate injections into each compartment for maximal nerve blockade. However, proximal connections between compartments have been identified, which may account for the success of single-injection techniques. Certain clinical observations may be interpreted as offering support or nonsupport for the existence of a functional tubular sheath. For instance, the relative success of multiple stimulation/injection axillary block techniques,[10] in addition to the failure of single-injection interscalene blocks, single-paresthesia axillary blocks,[11,12] or intraoperative catheter techniques,[13-17] to achieve complete anesthesia of the upper extremity could make the point against the classic description of a contiguous tubular sheath. Conversely, the 99%

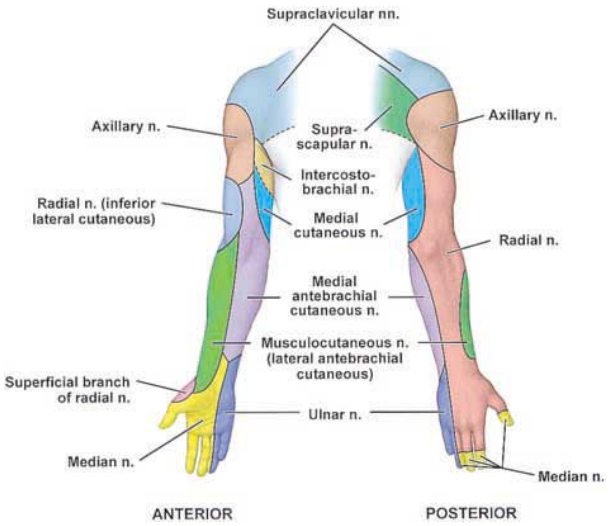

Fig 7. Cutaneous innervation of the upper extremity. (Reprinted with permission from Mayo Foundation.[50])

success rate of single-site injection transarterial axillary block reported in 1 study[18] speaks for the existence of a functionally unobstructed tubular configuration. There is no evidence of a sheath on cryomicrotome sections.[19] Recent research pertaining to axillary anesthesia has noticeably changed from reports of single, immobile needle techniques to those using multiple stimulations or injections.[10] Whether or not this reflects how contemporary researchers view the clinical importance of the axillary sheath is an interesting, but a speculative, question. Ultimately, a precise functional description of the axillary sheath and its clinical significance remains uncertain.

Nonbrachial Plexus Anatomy

Several nerves that are not part of the brachial plexus are of clinical importance in upper extremity and shoulder surgery because they may require separate blockade. The supraclavicular nerves (C3-C4) provide sensory innervation to the "cape area," extending to the second rib and encompassing the shoulder. The suprascapular nerve (C5-C6) sends sensory fibers to the posterior portion of the shoulder capsule, the acromioclavicular joint, and cutaneous innervation to the proximal third of the arm within the territory of the axilla. The intercostobrachial nerve originates from the second thoracic ventral rami (T2) and with the medial cutaneous nerve innervates the upper half of the posterior and medial skin of the arm (Fig 4).

Sensory and Motor Innervation of the Arm

The sensory and motor innervation of the upper extremity is clinically important for regional anesthesia practitioners. It determines which cutaneous nerve distributions within a surgical field require block, which terminal nerve branches require supplementation for a partially inadequate block, and helps to document the existence and distribution of pre- and postoperative neurologic deficits. Sympathetic nerve block results in increased blood flow to skin and muscle. This phenomena is more pronounced as one moves distally along the arm and increases hand blood flow by 296% compared with 132% with stellate ganglion block.[20,21] The cutaneous nerves of the upper extremity are a collection of neural fibers that originate from a variety of spinal cord segments and assigning cutaneous territory to a specific peripheral nerve is inconsistent, if not impossible (Fig 7). Motor innervation is clinically relevant as a means of matching a peripheral nerve stimulator (PNS)–induced motor response to which major nerve(s) has been stimulated. Superior trunk stimulation at the interscalene level results in shoulder elevation. Median nerve stimulation results in forearm pronation, wrist flexion, and thumb opposition. Ulnar nerve motor responses include ulnar deviation of the wrist, finger flexion, and thumb adduction. Wrist and finger extension are the hallmark of radial nerve stimulation. Because so much of the arm has multiple innervation, assessment of block efficacy is best accomplished by evaluating functions unique to each terminal nerve. A popular method of performing such an assessment is the 4 P's.[22] The patient is asked to *push* the arm by extending the forearm at the elbow against resistance (radial nerve), followed by resisting the *pull* of the forearm at the elbow (musculocutaneous nerve). The median nerve is assessed by the ability to distinguish a *pinch* at the palmar base of the index finger, followed by another *pinch* at the palmar base of the little finger (ulnar nerve).

Approaches To The Brachial Plexus

Clinicians have approached the nerves of the upper extremity at every anatomic division of the brachial plexus, from the level of nerve roots to that of isolated peripheral nerves.[23] Despite the existence of a myriad of techniques for each of these approaches, there are few clinical comparisons of block success rate and less still of latency or duration as a function of the chosen anesthetic approach and/or technique (Tables 1 and 2). Indeed, the very definition of success varies widely. Some studies have compared effective blockade of all nerves as the criteria for success, whereas others often compared adequacy for the intended surgical procedure (e.g., need for general anesthesia). In addition, few would argue that success is operator dependent, yet it is difficult to quantify and study this impression. Therefore, this section will collate the relatively sparse data pertaining to brachial plexus approaches and techniques. No attempt is made to describe individual approaches, but instead the reader is encouraged to seek this information at the ASRA Web site (www.asra.com) or refer to the cited original descriptions.

Interscalene Block

The principal indication for an interscalene block[24] (ISB) is surgery of the shoulder. Local anesthetic spread after interscalene administration extends from the distal roots/proximal trunks, and follows a distribution to the upper dermatomes of the brachial plexus and its upper trunk.[25] Consequently, ISB may functionally spare the C-8 and

Table 1. Comparison of Approaches to the Brachial Plexus

Author	Number of Subjects	Approach	Technique	Number of Injections	Criteria for Success	Percentage of Success (*P* value)
Supraclavicular versus axillary approach						
Brand 1961[202]	230	SCB	Paresthesia	NR	A	84
	246	AXB				92
						NS
Thompson 1988[203]	1913	SCB	Paresthesia	NR	A	83
	665	AXB				85
						NS
Moorthy 1991[38]	120	SCB	PNS	1	A	72
		AXB		NR		86
						NS
Kapral 1994[71]	40	SCB	Catheter	1	NR	95
		AXB		1		75
						NS
Fleck 1994[204]	40	SCB	PNS	1	A	80
		AXB	Paresthesia/ Transarterial	1		65
						NS
Infraclavicular versus axillary approach						
Kapral 1999[44]	40	ICB	PNS	1	N	90
		AXB		1		85
						NS
Koscielniak-Nielsen 2000[45]	60	ICB	PNS	2	N	53
		AXB		4		83
						($P = .003$)
Riegler 1992[52]	34	AXB	PNS	1	A	79
	79	SCB				97
	43	ISB				91
						NS
Schroeder 1996[55]	247	AXB	Multiple techniques	NR	A	89*
	59	SCB				78
	24	ISB				75
						(*$P < .03$)
Fanelli 1999[76]	1650	AXB	PNS	≤7	A	93
	171	ISB		≤3		94
						NS
Major variations of classic approaches						
Bouaziz 1997[48]	60	AXB	PNS	2	N	58
		AXB (humeral)		4		90
						($P < .05$)
Dalens 1987[205]	120	Parascalene	PNS	1	A	97
		SCB				88
						NS
Pippa 1992[58]	80	TCB	Fascial click	1	A	87
		AXB (classic)	Paresethesia			77
						NS
Pippa 2000[206]	60	SCB	PNS	1	A	86
		SCB				66
						NS

Abbreviations: SCB, supraclavicular; ISB, interscalene; TCB, transcoracobrachial; N, evaluation of individual nerve function; A, need for anesthesia supplementation; NR, not reported; NS, not significant.
*AXB versus SCB and ISB.

T-1 nerve roots (primarily the ulnar nerve, which may be spared in 50% of blocks[26]), making it a poor choice for hand and arm surgery (Fig 8). Several technical caveats pertain to ISB. First, paresthesia or muscle stimulation to the arm or anterior shoulder is appropriate for shoulder surgery.[27,28] Second, unintended evoked motor responses may guide needle placement. Contraction of the diaphragm indicates phrenic nerve stimulation and anterior placement of the needle tip. Alternatively, trapezius muscle stimulation indicates needle placement that is too posterior.

Suprascapular Nerve Block

The suprascapular nerve provides sensory innervation to 70% of the shoulder joint, especially the posterior and superior portion of the joint and cap-

Table 2. Comparisons of Techniques for Optimal Nerve Localization

Author	Number of Subjects	Approach	Technique	Number of Injections	Criteria for Success	Percentage of Success (*P* value)
Methods used to localize needles						
Tuominen 1987[207]	60	AXB	Catheter	1	N	60
			PNS			73
						NS
Goldberg 1987[11]	59	AXB	Paresthesia	1	N	80
			PNS	1		70
			Transarterial	2		79
						NS
Youssef 1988[60]	58	AXB	TA	1	NR	79
			Click/Paresthesia			90
						NS
Baranowski 1990[12]	100	AXB	Paresthesia	1-3	N	82
			PNS	1-3		72
			Catheter	1		56
						NS
Pere 1993[208]	50	AXB	PNS	1	A	96
			Transarterial	2		84
						NS
Schroeder 1996[55]	247	AXB	Paresthesia	NR	A	95*
			PNS			88
			Combination			94*
			Transarterial			81*
						*($P < .05$)
Rodriquez 1996[209]	40	AXB	Paresthesia	1	NR	95
			PNS			95
						NS
Koscielniak-Nielsen 1998[66]	100	AXB	PNS	4	N	88
			Transarterial	2		62
						$P < .0001$
Koscielniak-Nielsen 1999[67]	101	AXB	PNS	4	N	94
			Transarterial	2		64
						$P < .0001$
Inberg 1999[73]	50	AXB	PNS	2	N/A	92
				1		52
						$P = .02$
Sia 2000[62]	100	AXB	Paresthesia/infiltration	4	N	76
			PNS			91
						$P < .05$
Hunt 2001[210]	65	AXB	Paresthesia	1	A	85
			Paresthesia/Transarterial	3		85
				2		
			Transarterial			96
						NS
Number of injections						
Lavoie 1992[82]	90	AXB	PNS	4	A	93
				2		93
				1		50
						$P = .01$
Hickey 1993[69]	60	AXB	Transarterial	2	N	95
			(back and front)	1		
			Transarterial (back)	1		75
			Transarterial (front)			85
						NS
Koscielniak-Nielsen 1998[66]	80	AXB	PNS	3	N	90
				1		43
						$P < .0001$
Inberg 1999[73]	50	AXB	PNS	2	NR	92
				1		52
						$P = .02$
Koscielniak-Nielsen 1999[67]	106	AXB	PNS	4	N	87
				1		54
						$P < .001$
Coventry 2001[75]	60	AXB	PNS	3	NR	100
				2		90
						$P < .001$
Sia 2001[80]	84	AXB	PNS	4	N/A	90
			with ulnar stimulation	3		
			PNS			92
			without ulnar stimulation			NS

*Paresthesia or combination versus transarterial; combination included an elicited paresthesia or PNS response combined with transarterial injection.

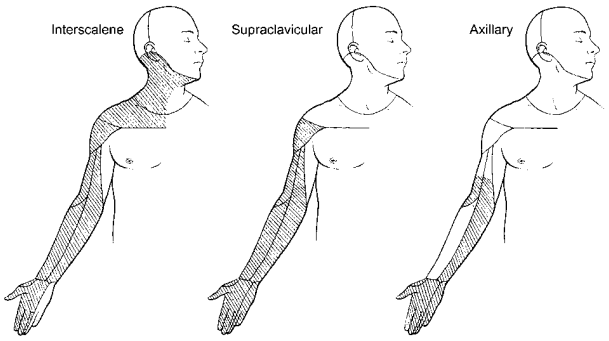

Fig 8. Typical sensory block patterns of various brachial plexus block techniques. (Modified and reprinted with permission from Mayo Foundation.[50])

sule.[29] This block[30] has been advocated for analgesia after shoulder joint surgery.[29]

Supraclavicular Block

The indications for supraclavicular block are surgery of the hand and arm. This block is performed where the brachial plexus is presented most compactly at the proximal division or trunk level. This compactness (Fig 5) may explain the block's historical reputation of providing short latency and the most complete and reliable anesthesia available for upper extremity surgery,[31] although confirmatory data do not exist. The 2 most commonly applied variations of the supraclavicular block are minor modifications of the classic (Kulenkampff[32]) and plumb-bob (vertical) approaches.[31,33] For hand surgery, stimulation of the middle trunk (hand contraction or paresthesia) has been associated with higher success rates.[34,35] The transarterial technique of injecting on both sides of the subclavian artery is unreliable and associated with a significant risk of hematoma.[36]

Intersternocleidomastoid Block

The intersternocleidomastoid block is indicated for hand and arm surgery. This block is a recently described variation of the supraclavicular approach. Although other supraclavicular approaches have been described (parascalene,[37] lateral paravascular[38,39]) this approach involves significant modifications, including a laterally directed needle placed between the heads of the sternocleidomastoid muscle.[40] This technique has been advocated for its ease of catheter insertion and theoretically a lower risk of pneumothorax, although the latter claim has not received extensive study. Intersternocleidomastoid block failed to achieve ulnar anesthesia in 15% of patients after a catheter technique.[40]

Infraclavicular Block

Surgery of the hand and arm are indications for the infraclavicular block.[41] The recently redescribed coracoid approach has revived interest in this approach.[42,43] In 2 comparative studies, infraclavicular block provided more consistent anesthesia for the axillary and musculocutaneous nerves than did axillary block,[44,45] but latency tended to be longer. The infraclavicular approach is not associated with changes in pulmonary function,[46] and there are no data pertaining to the risk of pneumothorax, although theoretically it should be minimal.

Axillary Block

The axillary block (AXB) is indicated for hand and arm surgery and is the most widely used, studied, and modified approach to the brachial plexus. All techniques—paresthesia seeking,[47] nerve stimulating,[48] perivascular,[49] and transarterial[18]—work at the level of the terminal branches. Successful block for each individual nerve varies from 60% to nearly 100% depending on the technique (Fig 8).[50] All of the previously mentioned techniques rely on the 4 nerves being in relatively close proximity to the axillary artery (Fig 6). Alternatively, the recently described midhumeral technique seeks individual evoked responses more distally, when individual branches have begun to course away from the artery.[48] The relationship of the musculocutaneous nerve to the brachial plexus deserves special consideration because it exits the plexus early and resides within the body of the coracobrachialis muscle at the axilla (Figs 4 and 6). Anesthesia of the musculocutaneous nerve is best assured by a separate injection into the belly of the coracobrachialis.[23]

Intercostobrachial Nerve Block

The intercostobrachial nerve is blocked separately when anesthesia is needed for the medial upper arm or axilla or for anterior portal placement during arthroscopic shoulder surgery (Fig 4).[50] Alternative approaches include local infiltration or T1-2 paravertebral block. Supplementation of this nerve is necessary because there are no convincing data confirming that any of the approaches to the brachial plexus consistently anesthetize the T1-2 nerve roots.[26] Placement of intercostobrachial block may prevent tourniquet sensation within the T1-2 distribution, but its importance in reducing tourniquet pain is controversial because tourniquet pain is likely mediated by ischemia and distal tissue compression in addition to local sensation.[51]

Comparative Efficacy of Brachial Plexus Approaches

Brachial plexus approaches provide a characteristic anatomic pattern of anesthesia (Fig 8). For example, PNS-induced motor response during interscalene block typically involves shoulder abduction and elbow flexion. These responses correspond to upper trunk (C5-C6) stimulation and typically anesthetize peripheral nerves that originate high in the plexus (supraclavicular, axillary, and musculocutaneous, rather than ulnar). Supraclavicular block anesthetizes middle and lower plexus nerves over 80% of the time (median, radial, and ulnar). AXB successfully anesthetizes distal terminal branches, spares the supraclavicular and axillary nerves, and variably blocks the musculocutaneous nerve.[26,52] Although it may seem logical that these patterns are linked to the successful provision of clinical anesthesia for specific surgical procedures, the impact of approach has not been prospectively studied in a reliable manner (Table 1).

Analgesia for Shoulder Surgery

Suprascapular nerve block (SSNB) has been investigated as an alternative method to interscalene block, an approach generally considered well suited for the provision of analgesia after shoulder surgery. A SSNB decreased pain and hospital stay after shoulder arthroscopy performed under general anesthesia[29]; however, these benefits were not seen in patients undergoing open shoulder surgery with supplemental SSNB and combined general/interscalene anesthesia (preliminary report).[53] Another preliminary report[54] noted that analgesia after shoulder arthroscopy was better with interscalene block as compared with SSNB and that both were superior to intraarticular infusion of local anesthetic.

Anesthesia for Arm and Hand Surgery

There are few randomized clinical trials comparing the efficacy of brachial plexus approaches for arm and hand surgery (Table 1). A retrospective comparison of interscalene, supraclavicular, and axillary blocks for elbow surgery found success rates of 75% versus 78% versus 89%, respectively.[55] Two prospective studies comparing coracoid infraclavicular (ICB) and AXB revealed conflicting results based on the number of nerves stimulated. Although single nerve stimulation resulted in similar success rates,[44] increasing the number of stimulated nerves improved AXB success over ICB.[45] Because the AXB technique received 4 stimulations/injections as compared with only 2 with the ICB approach, it is impossible to separate the influence of approach (ICB *v* AXB) from technique (2 *v* 4 injections). Similar interpretative difficulties are encountered in a report that 4-nerve stimulation midhumeral block provided significantly higher success rates than a conventional 2-nerve stimulation AXB.[48] Finally, in one of the few studies to consider cost and clinical outcome, Chan et al.[56] concluded that both brachial plexus block and intravenous regional anesthesia offered advantages over general anesthesia for hand surgery. Overall, existing data provide only limited insight into the ideal regional anesthetic technique for arm and hand surgery.

Techniques for Brachial Plexus Block

Methods of Needle Localization

With each anatomic approach to the brachial plexus, several methods of needle localization have been described for injecting after fascial clicks, mechanical paresthesia, electrical stimulation, transarterial injection, fanning injections, use of catheters, and using various imaging modalities. The following summarizes existing evidence for each of these localization techniques.

Fascial Clicks. The technique of relying on fascial clicks did not approximate needle to nerve in cadavers.[8] Four clinical studies have described success rates after fascial clicks with mixed results. High rates of successful surgical anesthesia have been described after a single injection of local anesthetic guided by fascial clicks during infraclavicular and transcoracobrachial approaches.[57,58] Conversely, rates lower than 85% were found when success in achieving anesthesia of all four peripheral nerves was sought after fascial clicks to guide AXB.[59,60]

Paresthesia Versus Peripheral Nerve Stimulation. Needle localization by either paresthesia or PNS appears to be equally efficacious. When directly compared, similar success rates (70%-90%) were reported for brachial plexus block, albeit these rates are generally lower than reported by others (Fig 9).[11,61] Obtaining 4 nerve stimulations with the midaxillary approach significantly increased overall success rate (91% *v* 76%) and reduced time for readiness for surgery when compared with eliciting three separate paresthesias and blindly supplementing the musculocutaneous nerve. However, in this study, only block of the radial nerve and the musculocutaneous nerve (blocked separately) were statistically different, suggesting that the techniques may be more similar than dissimilar.[62] When using a PNS, obtaining an appropriate motor response at $\leq$0.5 to 0.8 mA has been associated with a greater likelihood of successful block.[63,64]

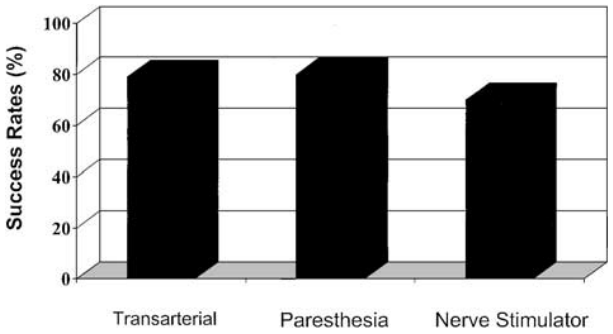

Fig 9. Comparative success rates of 3 axillary block approaches.[11]

Transarterial Injection Versus Paresthesia or Peripheral Nerve Stimulation. A 2-injection transarterial technique was just as successful (70%-80%) as a single-injection nerve stimulator[11,65] or a single-injection paresthesia technique (Fig 9).[11] When compared with a 4-nerve stimulation technique, the 2-injection transarterial technique for AXB was less predictable (90% *v* 62% success, respectively).[66,67] A single-injection, large volume (50 mL, 750 mg mepivacaine) transarterial technique described by Cockings et al.[18] was reported as 99% successful but was not directly compared with alternatives. Of note is the fact that this study is often cited as a single-injection technique, although 2 injections were actually made in the same location posterior to the axillary artery.

Perivascular Techniques. Whether by fanning or stable-needle injection(s), perivascular axillary block techniques are associated with high (88% and 99%) success and low complication rates.[18,49,68] In the Cockings et al. study[18] 50 mL of local anesthetic injected behind the artery resulted in 99% successful anesthesia, whereas in another study, single injection resulted in longer latency and/or less successful median nerve blockade compared with injecting in front of the artery or splitting the injection between the front and back.[69]

Imaging Techniques. Fluoroscopy[70] and ultrasound[71] have been used in brachial plexus anesthesia, yet no comparative clinical studies exist documenting unique advantage to these techniques. The use of ultrasound for brachial plexus anesthesia was recently reviewed, with the investigators concluding that it may have benefit in specific situations such as teaching or in patients with difficult anatomy.[72]

In summary, fascial clicks are a variously reliable method for needle localization depending on the approach chosen. Eliciting a paresthesia appears to be equivalent to using a PNS for accurate needle placement. Most, but not all, studies suggest that 2-injection transarterial techniques are equivalent to single paresthesia or single PNS techniques but that the later become more efficacious when multiple stimulations are used. Finally, needle localization using perivascular techniques is variably successful (62%-99%).

Single Versus Multiple Injections for Axillary Block

Whether multiple stimulation/injection techniques are superior to single-injection approaches is unclear (Table 2). AXB techniques using 2,[73] 3,[12,74] or 4 injections[75] have reported higher success rates, shorter latency, and/or more complete block compared with most, but not all,[18] reports using single injection. The advantages of multiple injection (94% success rate using less than 30 mL of local anesthetic) should be balanced against a reported 1.7% incidence of neuropraxia,[76] although this 1 month incidence figure compares favorably with the 3% to 8% incidence of nerve injury that others have reported 4 to 6 weeks postoperatively.[77,78] With regard to the ideal number of injections and/or stimulations sought with a PNS, several observations have been made. Two-nerve stimulation was just as effective for axillary block as 3-nerve stimulation, if the musculocutaneous nerve's sensory distribution was outside the surgical field.[79] Four-nerve stimulation took more time than 3-nerve stimulation and did not improve success.[80] Although multiple stimulations require more time, readiness for surgery may actually be faster.[66,67,81] Lastly, the specific nerves sought, not just their number, may be clinically relevant. Although the ideal nerves to stimulate vary,[75,80,82] the ulnar nerve appears to be the least important.[79,80] The efficacy of multiple-injection techniques for approaches other than AXB or ICB remains to be studied.

Continuous Techniques

Continuous nerve blockade using peripheral catheters is an evolving and exciting area of brachial plexus anesthesia, especially as a tool for postoperative analgesia. Despite growing clinical interest and technologic advancements, most current publications are clinical descriptions of several patients or case series of healthy outpatients undergoing ambulatory surgery.[83,84] Few studies have critically compared the clinical usefulness of brachial plexus catheter techniques to single injection or to other modalities of treating postoperative pain.[85-87] A contemporary review of continuous peripheral nerve blocks is available.[88]

Complications

As with any medical procedure, brachial plexus anesthesia is associated with risks. Large outcome studies of major complications after brachial plexus block are limited.[59,64,68,77,78,89-92] The incidence of various complications ranges from the extremely rare to the relatively common. For instance, a large study in France[89] included 21,278 peripheral nerve blocks in which the incidence of cardiac arrest (0.01%), death (0.005%), seizures (0.08%), and radiculopathy (0.02%) was extremely small. Anesthesia-related nerve injury (ARNI) accounted for 16% of total claims in the American Society of Anesthesiologists Closed Claims database.[92] Of these, 28% involved the ulnar nerve (only 15% were associated with regional anesthesia) and 20% involved the brachial plexus. Regional anesthetic techniques (axillary, interscalene, and supraclavicular approaches) were attributed specifically to only 16% of all brachial plexus injuries. Overall, the incidence of short- and severe long-term complications after interscalene block (catheter and single-shot techniques) is quite low (0.4%).[77] Moreover, regional anesthesia did not increase the risk of postoperative neuropathy in patients with preexisting ulnar nerve injury.[93] Less serious complaints are common. Indeed, over 50% of patients report at least 1 side effect after AXB, such as soreness (40%), transient numbness (11%), or bruising (23%).[91]

Peripheral Nerve Injury

Perioperative nerve injury is a potential, albeit rare, complication of regional anesthesia. Most nerve injury presents as residual paresthesia, hand or forearm hypoesthesia, and rarely as permanent paresis.[78,94] The overall incidence of long-term nerve injury ranges between <0.02% and 0.4%, depending on the definition of injury and length of follow-up.[78,89] The incidence of persistent ARNI decreases with time. Evidence of neurologic abnormality occurs within the first 24 hours in up to 19% of patients,[78] has decreased to 3% to 8% by 4 to 6 weeks,[77,78] and is well less than 0.5% by 1 year.[77] A substantial portion of neurologic injury becomes apparent in the early postoperative period, ranging from 21% presenting immediately after operation[92] to 100% within 48 hours of surgery.[89] Those deficits arising within the first 24 hours most likely represent extra- or intraneural hematoma, intraneural edema, or a lesion involving a sufficient number of nerve fibers to allow immediate diagnosis.[94,95] Subsets of ARNI present 1 to 28 days postoperatively.[77,92] In the Closed Claims database, median presentation was 3 days after surgery.92 Most injuries are evident by 3 weeks, although there are reports of delayed symptoms developing weeks after surgery.[68,77,89 ,92,94-96] The presentation of late disturbances in nerve function suggests an alternate etiology, such as a tissue reaction or scar formation leading to degeneration of nerve fibers.[94] It is not possible from available data to determine whether this reaction is because of mechanical trauma, local anesthetic neurotoxicity, or a combination of both.

Peripheral Nerve Injury and Brachial Plexus Block

Perioperative nerve injuries after upper extremity surgery may be the result of several contributing factors either unrelated or directly related to the regional anesthetic technique (Table 3). Unrelated risk factors include patient and surgical issues.[78,97] Regional anesthetic factors that may contribute directly to ARNI include mechanical trauma, ischemic injury, and chemical injury.

Mechanical Trauma: The Role of Needle Injury. Mechanical trauma, the role of needle type, and the elicitation of paresthesias have all been investigated as contributors to peripheral nerve injury.[68,78,95-102] Animal models have been used to examine needle type (long [14°] *v* short [45°] bevel) and bevel configuration.[100,102] Selander et al.[100] examined the immediate (2 hours) histologic implications of needle trauma in isolated or in situ rabbit sciatic nerves. Neuronal injury occurred more frequently with long-beveled needles compared with short-beveled ones. Whereas the overall frequency of nerve injury was less with short-beveled needles, injury severity was greater. Injury also varied in this study with bevel orientation, particularly with long-beveled needles, when transverse insertion caused

Table 3. Risk Factors Contributing to Perioperative Nerve Injury

Categories	Perioperative Risk Factors
Patient risk factors	Preexisting neurologic disorders
	Male gender
	Increasing age
	Extremes of body habitus
	Pre-existing diabetes mellitus
Surgical risk factors	Surgical trauma or stretch
	Tourniquet ischemia
	Vascular compromise
	Perioperative inflammation
	Postoperative infection
	Hematoma
	Cast compression or irritation
	Patient positioning
Anesthetic risk factors	Needle or catheter-induced mechanical trauma
	Ischemic injury (vasoconstrictors)
	Perineural edema
	Local anesthetic neurotoxicity

more severe injury compared with insertion parallel to nerve fibers. Rice and McMahon[102] also noted that long-beveled needles in the parallel configuration produced less intraneural damage than transverse long- or short-beveled needles, both immediately after injury and at 7 days. Importantly, by 28 days all injuries caused by long-beveled needles were resolving, and overall nerve injury scores were significantly lower, whereas those induced by short-beveled needles continued to display evidence of severe injury (Fig 10). They further showed that neural repair may be accelerated and more organized with long-beveled injuries, making long-term consequences less concerning. Rice and McMahon's approach[102] of evaluating long-term histologic and functional manifestations of injury may be more clinically relevant. Moreover, because multifasciculated rabbit nerve tended to slide away from needle tips, Selander et al's[100] model may overstate the protective effect of short-beveled needles. When fascicular impalement does occur, both studies agree that nerve injury is more severe with short bevels. There are no randomized clinical trials

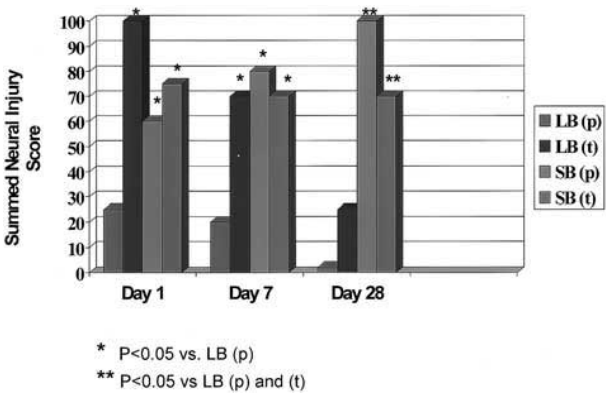

Fig 10. Percent of maximal rat sciatic nerve injury as a function of time, and needle bevel type and orientation. Nerve injury is determined by the cumulative score of three graded components: intraneuronal disruption (graded 0 to 5), axonal degeneration (graded yes / no), and disorganized fiber regeneration (graded yes / no). Nerve lesions induced by short bevel needles are more severe and take longer to repair than those induced by long bevel needles. Nerve injury induced by short bevel needle was often associated with persisting signs of injury 28 days after the injury. LB(p), long bevel needle in parallel configuration to nerve fibers; LB(t), long bevel needle in transverse configuration to nerve fibers; SB(p), short bevel needle in parallel configuration to nerve fibers; SB(t), short bevel needle in transverse configuration to nerve fibers. (Reprinted with permission of Oxford University Press/British Journal of Anaesthesia.[102] © The Board of Management and Trustees of the British Journal of Anaesthesia.)

(RCTs) to support or refute the ability of various needle types and bevel configurations to impale human nerves. Further clinical study is necessary before definitive recommendations can be made regarding the use of differently configured needles during peripheral nerve block.

Mechanical Trauma: The Role of Paresthesias. Whether the elicitation of a paresthesia represents direct needle trauma, thereby increasing the risk of nerve injury, is unknown. Clinical studies of paresthesia and ARNI have thus far been unable to definitively answer this question.[59,68,78,94,98,101] Selander et al.[94] reported a higher incidence of ARNI in patients when a paresthesia was intentionally sought during AXB compared with those undergoing a perivascular technique (2.8% *v* 0.8%, respectively; not significant). Because unintentional paresthesias were elicited and injected in patients within the perivascular group who then experienced ARNI, Winnie[103] has argued that these results do in fact become statistically significant. Forty percent of patients within the perivascular group reported unintentional paresthesias, showing the difficulty with standardization of technique, analysis of nerve injury, and perhaps most importantly, the futility of completely avoiding a paresthesia. Auroy et al.[89] also noted that all cases of radiculopathy after peripheral nerve block were associated with either a paresthesia during needle insertion or pain on injection (paresthesia or discomfort coincident with local anesthetic injection) and had the same topography as the associated paresthesia. In contrast to the previously mentioned observations, the American Society of Anesthesiologists Closed Claims Study found that only 31% of patients with persistent injury experienced paresthesia during needle placement or with local anesthetic injection.[92] Furthermore, a prospective investigation[78] using a variety of regional anesthetic techniques (transarterial, paresthesia, nerve stimulator) failed to associate complication rates with technique, an observation which has been confirmed by others.[59] Winchell and Wolfe[101] reported a 0.36% incidence of ARNI, despite 98% of patients experiencing a paresthesia. Although this incidence is at the higher end of reported ARNI, resolution occurred in all patients within 7 months. These studies would appear to support Moore's[104] contention that mechanical paresthesias are not per se an indication of nerve injury. The incidence of acute paresthesia may[78] or may not[93,95] be increased in patients with preoperative neurologic symptoms.[78] In summary, although elicitation of paresthesia during regional techniques is not definitively linked to ARNI, pain on injection does appear to heighten the risk of injury.

Does nonintraneural injection of local anesthetic after a paresthesia, or supplemental injection after a failed block, increase the risk of nerve injury? Injury did not occur when local anesthetic was injected through an axillary catheter, even though unintentional paresthesias were obtained during catheter placement in 39% of patients.[98] Similarly, there was no ARNI in patients who experienced a paresthesia during transarterial AXB when the needle was redirected before local anesthetic injection.[68] Because paresthesias may be attenuated, probing around a partially anesthetized nerve for the purpose of supplementing incomplete anesthesia may theoretically increase the risk of neural injury. Two studies support this concern. Sixty-seven percent of patients with deficits lasting >1 year[94] and 100% of patients with injury after transarterial AXB had received a supplemental injection.[68] Furthermore, techniques using multiple stimulations or paresthesia elicitation after partial injection of local anesthetic dose may theoretically increase the risk of nerve injury, but this question has received limited study.[76]

Ischemic Injury: The Role of Epinephrine and Neural Edema. The functional integrity of a peripheral nerve is highly dependent on its microcirculation,[105] which consists of an intrinsic supply of exchange vessels within the endoneurium and an extrinsic supply of larger, nonnutritive vessels (Fig 11).[106] Extrinsic circulation is under adrenergic control and thus highly responsive to epinephrine-containing solutions. For example, the topical application of plain 2% lidocaine reduced rat sciatic neural blood flow (NBF) by 39%, whereas adding epinephrine (1:200,000) resulted in an even greater (78%) reduction (Fig 12).[106] Whether or not such dramatic experimental reduction in NBF is clinically

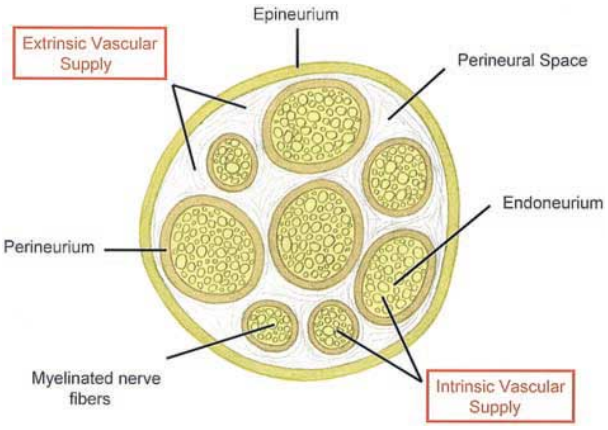

Fig 11. Cross section of a peripheral nerve with its vascular supply. (Reprinted with permission from Mayo Foundation.[50])

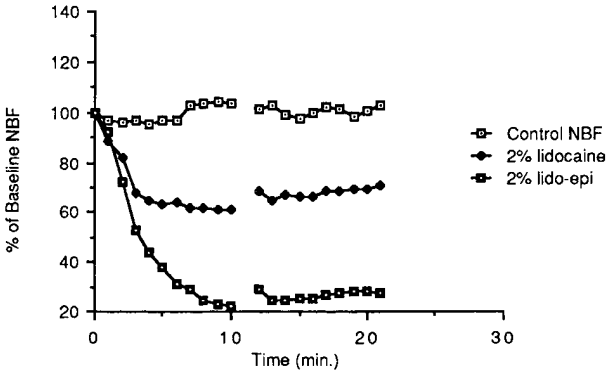

Fig 12. Effects of lidocaine 2% and lidocaine 2% with epinephrine on rat sciatic NBF. (Reprinted with permission.[106])

relevant in humans is unclear. Epinephrine is likely safe when applied to nerve bundles with intact barrier mechanisms but may accentuate injury in the event of barrier disruption or decreased NBF, such as may occur after an intraneural injection[99] or in individuals with chemotherapy-related neurotoxicity, diabetic neuropathies,[107] or atherosclerosis. Vast human experience suggests even these risks are decidedly quite remote, but there are no human RCTs that specifically evaluate adjuvant epinephrine as a factor contributing to ARNI.

Ischemic nerve injury may also occur after the intrafascicular (intraneuronal) injection of local anesthetics.[99,108] Intrafascicular injection may result in compressive nerve sheath pressures that exceed 600 mm Hg for up to 15 minutes. Elevated pressure interferes with endoneurial microcirculation[108] and may also alter the permeability of the blood-nerve barrier, resulting in axonal degeneration and axonal dystrophy. Subsequent fibroblast proliferation at the site of injury contributes to late-occurring changes in perineural thickness and endoneurial fibrosis.[109] These changes may result in delayed tissue reaction or scar formation, accounting for symptoms that develop days or even weeks after peripheral nerve blockade.[89,92,94-96]

Chemical Injury: The Role of Local Anesthetic Neurotoxicity. Clinical experience suggests that local anesthetic drugs are overwhelmingly safe when administered correctly and in the recommended concentrations. However, when inappropriately high concentrations, prolonged exposure times (i.e., continuous infusions; epinephrine use), or intraneural injections are encountered, severe degenerative changes may occur, leading to neurologic sequelae.[96,99,110] The persistent neurotoxic effects of local anesthetics are concentration dependent and seem to parallel anesthetic potency.[111] Acute phase (48 hours) histopathologic and functional effects

completely resolve 10 to 14 days later. These observations apply to histologic changes[112] as well as changes to compound action potentials[109,113] and occur in both long- and short-acting agents, with and without epinephrine. The recent popularity of continuous catheter techniques raises concerns about potential neurotoxicity from repeated perineural injection of local anesthetic. Kroin et al.[110] examined the neurotoxic effects of perisciatic injection of equipotent lidocaine doses repeated 3 times a day for 3 days in rats. Severe neurotoxicity occurred with 4% lidocaine only when rapid dilution of the drug was prohibited. Lidocaine 1% and 2% were innocuous in the model regardless of dilutional factors.

Regional anesthesia-induced nerve injury may in fact require a combined mechanical and chemical insult.[96,99,112] Selander et al.[99] showed that topical application of bupivacaine, with or without epinephrine, was innocuous in rabbits, whereas intraneural injection resulted in severe neural injury. Saline and plain 0.5% bupivacaine resulted in a similar degree of nerve injury, suggesting that injury was not from the injected test solution but rather was the result of injection trauma alone. However, higher concentrations of bupivacaine (1%) or the addition of epinephrine (1:200,000) to 0.5% bupivacaine resulted in significantly more severe axonal injury than saline or 0.5% bupivacaine alone. In contrast, Rice and McMahon[102] failed to document significant injury after saline injection alone. Thus, significant ARNI may require combined mechanical and chemical insult.

Diagnosis and Evaluation of Neurologic Complications. Patient, surgical, and anesthetic risk factors may all contribute to perioperative nerve injury (Table 3). Although most neurologic complications completely resolve within several days or weeks, significant injuries necessitate neurologic consultation to locate the lesion, document the degree of injury, and to coordinate further evaluation. Although it is often recommended to wait until evidence of denervation has appeared before performing neurophysiologic testing, a baseline study (including evaluation of the contralateral extremity) is often helpful in ruling out underlying pathology or a preexisting condition.[114] Furthermore, persistent symptoms may occur secondary to other readily treatable disease processes such as carpal tunnel syndrome or complex regional pain syndrome.[77]

The Role of the Peripheral Nerve Stimulator

The use of electrical stimulation to locate peripheral nerves was introduced in 1962.[115] Several advantages have been purported with this technique, including a higher success rate, the ability to perform procedures on sedated or uncooperative patients, the avoidance of vascular injury, and the avoidance of paresthesias and associated neurologic injury.[11,12,62,103,116-118] There is evidence that PNS can reduce the frequency of unintended paresthesia to around 15%[76,79] and facilitate readiness for surgery compared with paresthesia techniques.[66] However, there are no human RCTs that clearly support the assertion that PNS improves patient safety. Neurologic complication rates associated with PNS range from 0%[11,64,118] to more than 8%,[78] but within each of these investigations, there were no statistically significant differences between techniques (nerve stimulator, paresthesia, transarterial). Some advocates of the PNS approach argue that it facilitates performance of regional anesthesia on heavily sedated, anesthetized, or uncooperative patients because it purportedly provides exact needle localization without actually contacting nerve tissue. However, recent investigations have examined the relationship between a subjective paresthesia and an objective motor response elicited by a PNS in patients undergoing interscalene or axillary blockade.[63,119] Nearly 25% of patients initially reporting paresthesia required a current >0.5 mA to manifest a motor response, suggesting an inconsistency of elicited motor responses despite the needle presumably being near a nerve. Concerns were therefore raised that awareness of a paresthesia subsequent to needle advancement could be compromised in sedated or anesthetized patients, thus potentially subjecting them to unrecognized intraneural injection.[63,120,121] Such concerns are further validated by reports of nerve injury after low current (<0.5 mA) electrical stimulation[89] and intramedullary injection during the course of PNS-assisted interscalene block in patients under general anesthesia (Fig 13).[122] Therefore, the assertion that nerve stimulation allows clinicians to approximate neural structures without the risk of mechanical trauma does not appear to be valid. As noted by Urmey[120] in a recent editorial, although PNS may be a valuable technical adjunct for performing brachial plexus blocks, it is not a substitute for detailed anatomic knowledge and careful technique.[120]

In summary, ARNI remains a rare but poorly understood complication of brachial plexus anesthesia. Our lack of knowledge is underscored by the absence of human RCTs of sufficient statistical power to confidently link risk to outcome. Most previously proclaimed admonitions for eschewing ARNI, such as short-beveled needles, avoidance of paresthesia, or use of a PNS, have little evidence on which to base their acceptance. Nevertheless, certain risk factors for ARNI emerge from analysis of

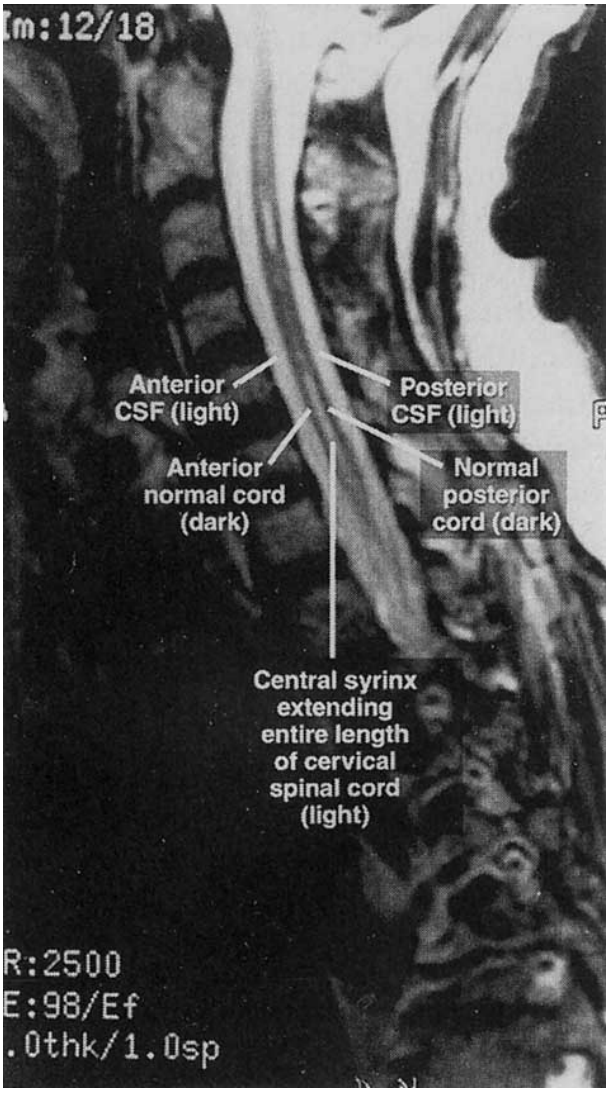

Fig 13. Magnetic nuclear resonance scan of cervical spinal cord injury (central syrinx and hemorrhage) secondary to intramedullary injection of local anesthetic. (Reprinted with permission.[122])

accumulated evidence. These include the clear damage caused by intraneural injection, the worsening of injury by local anesthetics or epinephrine when structural integrity of the peripheral nerve has been compromised, and the potential danger of performing plexus blocks in anesthetized or heavily sedated patients.

Vascular Injury

Vascular complications are rare but potentially devastating events that are reported with varying frequencies during interscalene, supraclavicular, infraclavicular, or axillary block. Unlike the known risks of spinal hematoma arising from concomitant anticoagulation and neuraxial block, risk for brachial plexus vascular injury in anticoagulated patients is neither clearly defined nor are there guidelines available. If increased risk is presumed, brachial plexus blocks in coagulopathic patients should be based on careful risk/benefit analysis and performed cautiously, especially if an expanding hematoma could compress the airway or be difficult to access.

Transient vascular insufficiency is a reported complication of brachial plexus block, occurring in up to 1% of patients.[68] Vasospasm may occur after arterial puncture or as a consequence of local anesthetic-induced vasoconstriction.[123] Treatment includes intraarterial lidocaine (being mindful of total dose to avoid high local anesthetic plasma levels), topical warming, or nitroglycerin paste.[124] The risk of hematoma immediately after brachial plexus techniques is small (0.001 to 0.02%),[64,68,125,126] although the incidence may increase at 1 month follow-up.[64] Although most are inconsequential, hematomas may[126] or may not[78] be associated with postoperative paresthesias or transient nerve injury. Pseudoaneurysm formation is another rare complication of brachial plexus block, occurring most commonly within the axillary artery.[127] Pressure-induced neural ischemia with subsequent neurologic impairment may occur because of the close proximity of neurovascular structures within the axilla. Risk factors include the extent of the injury (number of needle punctures), impaired vascular elasticity, diabetes mellitus, and hypertension, with isolated occurrences in anticoagulated patients.[127] Axillary artery dissection has been reported as a result of intramural injection of local anesthetic.[128] Thus, vascular complications are rare after brachial plexus block but must be considered in patients with postoperative neurologic impairment. Early recognition and prompt surgical intervention are critical to avoid long-lasting neurologic sequelae.

Muscle Injury

Myonecrosis from local anesthetics at concentrations typically achieved at the site of injection is well proven and characteristic of all local anesthetics, with bupivacaine producing the most intense effect. Because damage is dose related, continuous local anesthetic administration may worsen injury. Epinephrine and steroid also intensify this effect, which produces immediate and complete destruction of adult myocytes. Because local anesthetic myotoxicity is dependent on a nonspecific increase in sarcoplasmic reticulum permeability to calcium, immature myocytes are spared because they lack an

internal calcium reservoir. Thus, new muscle regenerates over 3 to 4 weeks.[129]

Hemidiaphramatic Paresis

The proximity of the phrenic nerve to the interscalene groove frequently leads to unintended local anesthetic block and resultant diaphragmatic dysfunction. The frequency and clinical relevance of this side effect vary with block site but should be carefully considered when providing above the clavicle techniques in patients with underlying pulmonary disease. The incidence of hemidiaphragmatic paresis (HDP) is 100% after interscalene brachial plexus block.[130-136] Some patients will report mild dyspnea or altered respiratory sensations and may experience 25% to 32% reduction in spirometric measures of pulmonary function.[131] The development of HDP and pulmonary function changes are not altered by the application of digital pressure during block injection, reducing the local anesthetic volume [132,137] or both.[134] Abnormal diaphragmatic function persists in 50% of patients after 24 hours of dilute bupivacaine continuous infusion.[135] Ropivacaine's purported ability to preserve motor function is also not protective,[136] although in a continuous catheter study, diaphragmatic and pulmonary functions were similar to a patient-controlled intravenous opioid group.[85] Supraclavicular block has a lower incidence of HDP compared with the interscalene approach (50%, 95% confidence interval: 14 to 86%) and is not associated with respiratory symptoms or change in pulmonary function.[138] ICB is not associated with pulmonary function changes.[46] Because HDP occurs in all patients given interscalene block and happens unpredictably after supraclavicular block, neither approach is recommended in patients unable to tolerate a 30% reduction in pulmonary function.

Pneumothorax

Pneumothorax is the most serious complication associated with supraclavicular brachial plexus block, including the intersternocleidomastoid approach. It has also been reported after interscalene[77] and suprascapular block and might rarely occur with infraclavicular approaches. The reported incidence of pneumothorax after supraclavicular block is 0.5% to 6.1%.[23,139,140] This may be higher than actually seen in contemporary practice because most reports stem from experience with classical supraclavicular approaches, wherein the anesthetizing needle is guided toward the apical pleura (Fig 5).[139,140] The plumb-bob and first rib palpation approaches were designed in part to lessen the risk of pneumothorax,[31,141] although no large controlled studies confirm this contention. The incidence of pneumothorax is likely reduced by operator experience; using shorter needles; and extra care with tall, thin patients who are more likely to have high apical pleural reflections or in patients with emphysema. Patients who develop pneumothorax are not likely to report symptoms for 6 to 12 hours (in the absence of positive pressure ventilation). This implies a futility of early chest radiographs and raises concerns about performing these blocks on outpatients with problematic medical follow-up. Many patients report only mild symptoms, primarily pleuritic chest discomfort.[139] Diagnosis of pneumothorax is confirmed by a chest radiograph taken during full exhalation.

Local Anesthetics: Unintended Destinations

Intravascular Injection. The proximity of the brachial plexus to vascular structures contributes to the intravascular injection of local anesthetic. This complication was found to occur in 0.2% of patients receiving transarterial axillary block in 1 study, even with test dosing and aspiration.[68] Intraarterial injection can be suddenly expressed when associated with interscalene or supraclavicular block because local anesthetic injected directly into the vertebral or carotid artery, or retrograde flow of local anesthetic via the subclavian artery, may proceed directly to the brain. The estimated convulsant doses after unintended carotid or vertebral artery injection are lidocaine 14.4 mg and bupivacaine 3.6 mg. Symptomatic toxicity has been reported at similar doses.[142] Intravenous injection is less worrisome because larger volumes may be tolerated before toxicity. The absorption rate of local anesthetic does not appear to vary as a function of brachial plexus block approach.[143] What constitutes the maximum safe recommended local anesthetic dose for brachial plexus anesthesia is controversial and poorly grounded in evidence.[144] Peak arterial plasma levels of local anesthetics do not correlate with body surface area or patient weight (Fig 14).[50] Despite manufacturer's recommended dosages, there are multiple published reports of significantly higher doses delivered near the brachial plexus without adverse sequelae, although the safety of this practice is not well studied.[18,26] Importantly, local anesthetic toxicity may become problematic in patients with compromised pharmacokinetics secondary to congestive heart failure, advanced age, hepatic failure, or with continuous techniques.[125] Total doses in these patients should be reduced but to what extent is poorly defined.

The frequency of seizure after peripheral nerve block is 5 times more likely to occur compared with

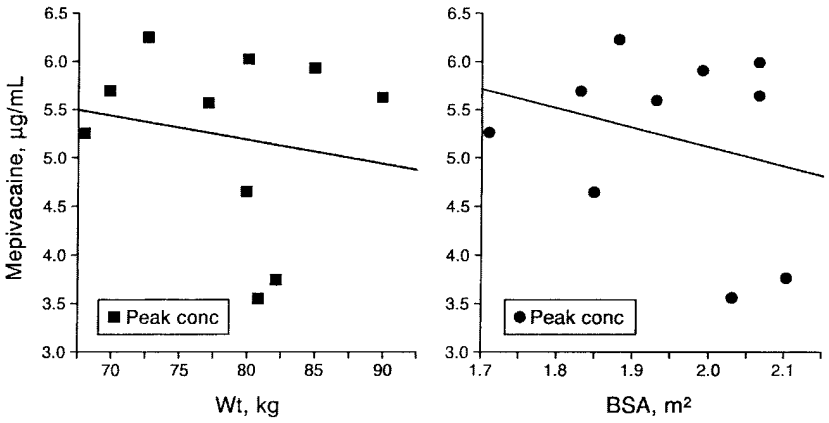

Fig 14. Peak concentrations of mepivacaine do not correlate with weight in kilograms (Wt, kg) or body surface area (BSA, m^2). (Reprinted with permission from Mayo Foundation.[50])

epidural injection.[89] This scenario is best avoided by meticulous aspiration and fractionated dosing with continuous observation for signs and symptoms of local anesthetic toxicity, understanding that these maneuvers are not totally reliable. The seizure rate per 1,000 patients varies according to the brachial plexus approach selected—1.2 to 1.3 for axillary (just as likely to occur with a transarterial, peripheral nerve stimulator, or midhumeral technique[64]), 7.6 for interscalene, and 7.9 for supraclavicular. Compared with seizures, the risk of cardiovascular collapse after unintentional intravascular injection is less certain. Animal studies suggest a margin of safety afforded by lidocaine over longer-acting agents (safety ratio of 1:2:9, representing bupivacaine:levobupivacaine/ropivacaine:lidocaine, respectively). The safety profile of levobupivacaine compared with ropivacaine is less clear.[145,146] Large epidemiologic studies of various peripheral nerve blocks report seizures after unintended intravascular injection of racemic bupivacaine but not cardiac arrest.[89,90] Although cardiovascular collapse undoubtedly occurs, it is seldom reported.[142] Most importantly, anesthesiologists should understand that the risk of intravascular injection with subsequent seizure is very high with brachial plexus anesthesia, perhaps exceeded only by caudal anesthesia.[90]

Subarachnoid or Epidural Injection. Local anesthetics intended for the brachial plexus may spread to the neuraxis. Interscalene brachial plexus block has been linked to unintended subarachnoid block and to cervical or thoracic epidural block.[23,147] Needle entry into the subarachnoid space can occur directly or uncommonly via the dural cuff or injection into the nerve or ganglion. These complications are best avoided by using shorter needles, by directing the needle slightly caudad to avoid the intervertebral foramen, by slow/fractionated injection, and perhaps by lower volumes. Cadaver studies emphasize the nearness of the neuraxis to an interscalene block needle (Fig 15). The minimum distances from skin to the C6 foramen and vertebral column are 23 mm and 35 mm, respectively.[147]

Cervical Sympathetic Chain. Excessive local anesthetic spread can also affect the cervical sympathetic chain, causing the patient to manifest Horner's syndrome. This side effect occurs with interscalene[148] and especially supraclavicular block, with a reported 20% to 90% incidence.[23,34] Other than educating patients regarding the temporary nature of this phenomenon, there is generally no harm from its occurrence. Although lower injectate volume may logically decrease the likelihood of Horner's syndrome, this association is unproven.[137]

Recurrent Laryngeal Nerve. Hoarseness may transpire after interscalene block[23,148] or after 1.3% of supraclavicular blocks.[34] It happens as a consequence of excessive local anesthetic spread to the recurrent laryngeal nerve or airway edema. Hoarse-

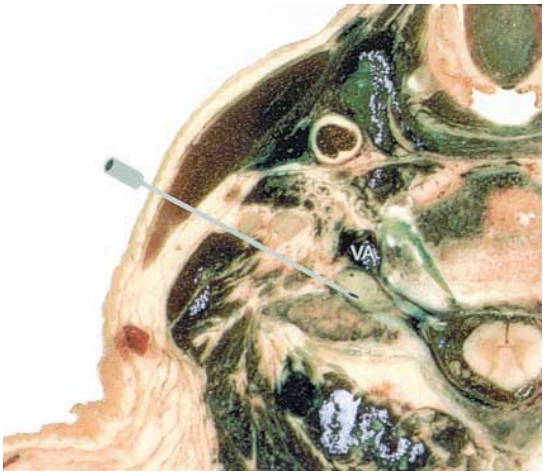

Fig 15. Cryomicrotome axial section of the left neck (anterior is up), showing the proximity of the brachial plexus to the dorsal root ganglia (needle) and the nerve root cuff just medial to this, as well as the epidural and subarachnoid spaces within the spinal canal.

ness may occur in conjunction with Horner's syndrome[148] and, again, is primarily a nuisance side effect that is best treated with patient reassurance.

Hypotensive/Bradycardic Events

Severe, sudden hypotensive and/or bradycardic events (HBE) have been reported in 13% to 24% of awake sitting patients undergoing shoulder arthroscopy with interscalene brachial plexus anesthesia.[149,150] Possible etiologies of HBE included β^1-agonist effects of exogenous epinephrine and activation of the Bezold-Jarisch reflex.[151] This reflex occurs when the combination of decreased venous return and heightened sympathetic tone leads to forceful contraction of a near-empty left ventricle, with consequent parasympathetically mediated arterial vasodilation and bradycardia. The incidence of HBE is decreased when prophylactic metoprolol, but not glycopyrrolate, is administered after block placement in 2.5 mg increments to an endpoint of either heart rate $<$60 bpm or maximal dose of 10 mg.[151] Clinically, HBE is unpredictable, typically occurring 61 $\pm$ 18 minutes after block placement and often heralded by lightheadedness or nausea.[149] The vast majority of these events are reported in awake patients. Whether or not the frequency is different in patients under general anesthesia or a combined technique is unknown.

Limb Protection and Discharge Criteria. There is a paucity of RCT data regarding limb protection and discharge criteria after brachial plexus block.[152] Long-acting blocks theoretically increase the risk of nerve injury secondary to prolonged immobility.[78] However, it is generally safe to discharge patients with partial sensory block,[153] assuming proper instruction to avoid potential sources of injury.[118] Patients with residual upper extremity sensory and/or motor blockade should be properly fitted with a sling or similar protective device. Instructions should include a warning to protect the insensate limb from pressure or thermal injury and advice as to when to expect sensory block resolution. As an alternative to long-acting blocks, the midhumeral approach allows for selectively anesthetizing individual nerves to achieve faster motor block resolution while maintaining prolonged analgesia of nerves within the surgical site.[152] Selective application of clonidine also prolongs analgesia without motor block.[154]

Tourniquet Effects

Occlusive tourniquets are applied to the upper extremity to improve the surgical field. Ischemic nerve or muscle damage is unlikely in the noncompressed area if flow is reestablished within 6 hours, but damage may occur under the cuff within 2 to 4 hours.[155] Up to 40 minutes are necessary to reach normal metabolic status after 3 hours of tourniquet inflation.[156] Tourniquets produce pain by a complex mechanism, most likely involving neural ischemia.[157] Reperfusion almost immediately relieves tourniquet pain, although a transient second phase (not usually seen with regional techniques) may ensue.[158]

Pharmacologic Considerations

Local Anesthetics

Few large, controlled studies compare various local anesthetics for brachial plexus block. Analysis of these studies is difficult by virtue of the many possible variations during a brachial plexus block procedure including which block technique is chosen, which adjuvant is added, what is the pH of the injected solution, how is duration defined and measured, the surgical model, and individual patient characteristics. Despite these limitations, available literature provides insight into how local anesthetic agent selection, dose, concentration and volume, and physical modifications can affect onset, spread, quality, and duration of anesthesia.

Local Anesthetic Selection. Selecting a specific local anesthetic for brachial plexus anesthesia should be tailored to specific goals. In general, the intermediate-acting agents lidocaine and mepivacaine demonstrate faster onset and lower failure rates than bupivacaine or ropivacaine but at the expense of shorter analgesic duration.[55,159] Whether or not prolonged analgesia is desirable depends on how much the patient desires a numb extremity, the ability to adequately protect an insensate arm from injury, and the surgeon's need to assess neurovascular function. Recent studies compare the newer local anesthetics ropivacaine and levobupivacaine to racemic bupivacaine. Sensory and motor block onset and duration was not different with plain 0.75% ropivacaine compared with plain 0.5% bupivacaine.[160,161] As ropivacaine concentration was increased from 0.5% to 0.75% to 1%, onset times became faster, but sensory and motor block success rates and analgesic duration did not differ from 0.5% bupivacaine.[162,163] Thus, 0.75% ropivacaine or 0.5% bupivacaine appear to be quite similar for brachial plexus anesthesia and analgesia. In a single comparative study of brachial plexus anesthesia, levobupivacaine has block characteristics similar to racemic bupivacaine.[164]

Dose, Concentration, and Volume. The onset, intensity, and duration of any regional anesthetic is ultimately determined by the mass of injected local anesthetic (mass = concentration $\times$ volume).[165]

Clinical support for this concept comes from the observation that the onset of AXB is proportional to the logarithm of local anesthetic concentration.[5,163,166] Whether increasing local anesthetic mass results in a higher success rate is controversial. In a series of studies involving continuous AXB using 1% mepivacaine with epinephrine, Vester-Andersen et al.[13-17] systematically evaluated the role of volume, concentration, and dose on block efficacy. When dose was held constant, increasing volume from 20 to 40 to 80 mL had little effect on sensory blockade of most nerves,[14] although motor block was superior at lower volumes, probably reflecting a concentration effect.[14,16] When volume was constant, sensory blockade was only 70% to 100% successful in all nerve groups, regardless of increasing concentration (0.5% to 1% to 1.5%).(15) Increasing the dose from 400 to 500 to 600 mg mepivacaine resulted in no difference in sensory or motor anesthesia.[15] Ultimately, in this catheter technique model, isolated changes in volume, concentration, or dose had little effect on sensory nerve blockade. Only the combination of increasing volume and drug mass showed minor improvements in block quality. This series of studies is generally supportive of the concept that drug mass is the most important determinant of block efficacy, although even it has relatively little impact on anesthetic success.

Local Anesthetic Mixtures. Mixtures of local anesthetics are intended to provide faster block onset than long-acting agents and to extend the duration typically seen with intermediate- or short-acting agents. Overall, mixtures provide few clinically significant advantages[165] but instead result in a profile similar to a pure intermediate-acting agent. Furthermore, combined administration of local anesthetics produce epileptogenic effects that are additive.[167] A more elegant approach involves selective application of different local anesthetic agents or clonidine[154] to individual nerves. By injecting lidocaine on musculocutaneous and radial nerves and bupivacaine on median and ulnar nerves, one can achieve faster recovery of motor block but longer analgesic duration comparable to injecting a mixture of lidocaine and bupivacaine on all 4 nerves.[152]

Physical Manipulations. Certain physical manipulations of local anesthetic solutions have been evaluated as methods to improve brachial plexus block onset or spread. Alteration of local anesthetic temperature has contradictory effects. Injecting ice-cold lidocaine hastens block onset and increases duration but is painful.[168] Warming local anesthetic to 37°C may[169] or may not quicken onset time.[170] Because local anesthetic blockade of sodium channels is in part use dependent, exercising the arm after block placement significantly speeds anesthesia onset but does not prolong duration.[171] Rapid injection of local anesthetic reduces anesthetic spread and increases failure rate.[172] Firm digital pressure during the time of injection neither reduces the incidence of hemidiaphragmatic paresis[133,134] nor improves block spread with the interscalene[133] or axillary approach.[13] Finally, abduction of the arm to 0° increases local anesthetic spread centrally, but does not affect sensory blockade.[173]

Alkalinization of Local Anesthetics

Clinical studies are inconclusive regarding alkalinization of local anesthetics as a means of hastening block onset, although animal studies suggest that doing so may compromise duration and quality of block.[174] The presence or absence of epinephrine is a central dividing point for alkalinization analysis. Most clinical studies of alkalinizing local anesthetic with epinephrine mixtures have shown a reduction in onset time.[175-177] Alkalinization appears most effective with commercially prepared epinephrine-containing local anesthetics, probably because these solutions are formulated at a lower pH. Thus, the relative effects of raising pH are larger than with plain local anesthetic solutions. Indeed, when fresh epinephrine is added to plain lidocaine, onset times of brachial plexus anesthesia with alkalinization are similar to those seen without.[178] The clinical significance of faster onset is questionable. For instance, adding sodium bicarbonate to mepivacaine with epinephrine significantly decreased sensory block onset time from 1.8 ± 0.2 minutes to 1.0 ± 0.2 minutes.[175] Effects on other block characteristics are similarly unconvincing. For example, alkalinization does not improve sensory block success rate[177,178] nor does it affect plasma mepivacaine levels in the absence of epinephrine.[179] There are no well-controlled clinical observations of the impact of alkalinization on peripheral nerve block intensity and duration, but in rats, alkalinization of plain 1% lidocaine decreased block intensity by 25% and decreased block duration by over 50%. Similar effects were not observed with 1% lidocaine with epinephrine.[174] In summary, clinical data do not support the alkalinization of local anesthetics used for brachial plexus blockade. There appears to be little reason to admix sodium bicarbonate with plain local anesthetics or to those with freshly added epinephrine. Indeed, doing so may decrease block duration and intensity. Alkalinization of commercial preparations of local anesthetics with epinephrine may hasten onset enough to gain statistical significance, but anesthesiologists must decide if

saving 1 to 3 minutes is clinically relevant in their practice.

Epinephrine

Epinephrine prolongs duration and intensity of most local anesthetics used for peripheral nerve block. For example, 1:200,000 dilution (5 μg/mL) significantly increases the mean duration of lidocaine (264 minutes with *v*186 minutes without epinephrine). These effects are caused by vasoconstriction, which prolongs the nerve's exposure to local anesthetic drug mass by limiting clearance.[180] Other benefits of epinephrine include acting as a marker of intravascular injection[165] and potentially limiting systemic local anesthetic toxicity by reducing time-to-peak concentration and peak plasma concentration. Adjunctive epinephrine is most effective with lipophobic local anesthetics such as mepivacaine or lidocaine when it prolongs anesthetic duration in a dose-dependent manner up to a 1:200,000 dilution. Stronger concentrations are associated with hemodynamic side effects including increased heart rate and cardiac output and decreased peripheral vascular resistance. A 1:400,000 dilution slightly decreases block duration (240 minutes *v* 264 minutes with 1:200,000 dilution)[181] and does not decrease nerve blood flow.[182] Routine use of adjunctive epinephrine clearly prolongs brachial plexus block duration with little, if any, risk. However, on a theoretical basis with some supporting animal data, anesthesiologists may prefer to use weaker concentrations (1:400,000) or avoid epinephrine altogether in patients at risk for cardiac ischemia or potentially prone to nerve injury as a consequence of decreased blood flow from chemotherapy, diabetes, or atherosclerotic disease.

Opioids

Peripheral opioid effects have been shown with intraarticular injection and with wound infiltration, but the clinical relevance of peripheral (brachial plexus) opioid receptors is uncertain.[183,184] This lack of basic science clarity extends to the clinical effects of adjunctive opioids used with brachial plexus block. Interpretation of clinical studies is difficult because many lack a control group from which to separate the possibility of systemic opioid effect. Indeed, as the quality of study improves, the evidence for a clinically significant peripheral opioid effect at the brachial plexus diminishes. Brachial plexus studies that include a systemic control group mostly fail to show compelling reasons to add opioids to anesthetizing solutions, most often finding no significant differences in onset, duration, block quality, or pain scores.[185-187] Recent reviews of the role of opioids in peripheral nerve block conclude that their anesthetic and analgesic effects are not clinically relevant.[188,189] If there is a role for additive opioid, it may be the addition of morphine or buprenorphine to intermediate-acting local anesthetics as a means of prolonging analgesic duration, although evidence for this benefit is conflicting.[183-185,187]

Clonidine

Clonidine is second only to epinephrine as a useful adjuvant for brachial plexus blockade. Strong clinical evidence supports its use and has been recently reviewed.[189,190] Prolongation of anesthesia and analgesia with brachial plexus clonidine is likely peripherally mediated[154] and dose dependent, as is its side effect profile. Brachial plexus clonidine 150 μg delays the onset of pain by 2-fold when compared with systemic control,[191] and 0.5 μg/kg prolongs analgesia by 50% compared with placebo (492 *v* 260 minutes). When added to mepivacaine, the minimum dose required to prolong anesthesia is 0.1 μg/kg, whereas that needed to prolong analgesia is 0.5 μg/kg. Side effects (hypotension, decreased heart rate, sedation) do not occur up to a dose of 1.5 μg/kg[192] or a maximum dose ≤150 μg.[192-195] Once pain occurs, the presence of clonidine does not alter its intensity.[191,192,196] Clonidine does not affect tourniquet pain.[193] The choice of local anesthetic affects the efficacy of clonidine. Dose-dependent prolongation of clonidine admixed with mepivacaine or lidocaine is well established,[190] but its ability to increase analgesic duration after brachial plexus blocks with long-acting local anesthetics is less clear. Whether clonidine is better than or adds value to epinephrine-containing mixtures is uncertain.[195,197]

Other Adjuvant Drugs

Tramadol, an analgesic with peripheral effects similar to clonidine, moderately increases sensory block duration when compared with placebo or systemic control.[198] Brachial plexus verapamil offers little advantage over epinephrine if the expected surgical duration is <3.5 hours.[183] Neostigmine does not improve sensory or motor block qualities but is associated with a 30% incidence of gastrointestinal side effects.[199] Hyaluronidase does not hasten block onset, reduce the incidence of failed block, or affect local anesthetic blood concentration, but it does shorten block duration.[140,200] To date, there have been no studies evaluating nonsteroidal anti-inflammatory drugs as adjuvants for brachial plexus block.[201]

In summary, local anesthetic and adjuvant selec-

Table 4. Suggested Future Directions for Brachial Plexus Anesthesia Research

Goal for Knowledge Improvement	How Might This Goal Be Accomplished?
Obtain meaningful comparative outcome, safety, and cost data	Appropriately powered RCTs
Improve methods to enhance postoperative analgesia	Development of continuous techniques Development of long-acting local anesthetic formulations Improved equipment
Reduce peripheral nerve injury and vascular complications	Neurophysiologic methodologies Real-time imaging
Improve teaching of brachial plexus anesthetic techniques	Virtual reality Computer simulation/modeling
Optimize local anesthetic and adjuvant selection	Neurophysiologic methodologies Appropriately powered RCTs
Optimize needle-to-nerve placement	Imaging techniques
Improve our understanding of peripheral nerve stimulators	Neurophysiologic methodologies Improved equipment

tion, as well as dosing, clearly affect brachial plexus block characteristics. Yet, despite our ability to modify local anesthetic solutions, it is unclear to what extent block spread and quality is more a function of technical intervention than pharmacologic adjustment. Whereas no studies evaluate the pharmacologic contributions of local anesthetic and adjuvant selection versus the technical issues of block selection and performance, anesthesiologists should be aware that both profoundly affect the success of brachial plexus anesthesia.

Future Research Directions

Nearly 120 years have passed since the first application of cocaine to the brachial plexus. As one speculates where the next decade of research should take us, several directions seem appropriate (Table 4). The exponential innovation in imaging modalities opens many doors for furthering our understanding of brachial plexus anesthesia, offering opportunities not only to better understand anatomic infrastructure but how to match a specific technique to a clinical goal. Such imaging will likely improve our ability to accurately approximate needle to nerve, but an even greater value may be in promoting the understanding of local anesthetic spread or real-time views of the dynamics between needle tip, nerve fascicles, and surrounding vascular structures. Neurophysiologic methodologies may also increase our knowledge of nerve conduction, thereby giving us a more objective tool to evaluate various pharmacologic agents for promoting rapid anesthetic recovery while extending analgesia. Yet, despite the promise of technologic advancement, researchers should strive not to merely describe another technique but to adequately, fairly, and powerfully compare new and existing techniques in a manner consistent with meaningful outcome analysis. As an example, the contemporary growth of continuous peripheral techniques challenges our very resolve to investigate outcome, cost, and effectiveness rather than simply to incorporate a new technique or piece of equipment into our practice. Indeed, one wonders if anesthesiologists really need another brachial plexus technique as much as they need reliable comparative information on the tools we already possess. Continued efforts are required to understand the etiology and prevention of 2 serious complications of brachial plexus anesthesia: peripheral nerve injury and local anesthetic systemic toxicity. Such inquiry will require vastly improved randomized clinical trials that have sufficient power and control to provide us with evidence-based information to guide our practice. Until such time, answers to even simple practical questions, such as the ideal number of stimulations or injections to optimize AXB, will remain elusive. Finally, to what extent will virtual reality and computer modeling compliment hands-on learning at the bedside? The future challenges us to devise better ways to train residents and practitioners alike in the art and science—or dare we say, the science of brachial plexus anesthesia.

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