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Current Issues in Spinal Anesthesia

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SPINAL anesthesia has enjoyed a long history of success and recently celebrated a centennial anniversary.[1] Anesthesiologists master spinal anesthesia early during training with achievement of competence (> 90% technical success rate) after only 40–70 supervised attempts.[2,3] The ease and long history of spinal anesthesia may give the impression that it is a simple technique with little sophistication. However, much has been learned recently regarding the anatomy, physiology, pharmacology, and applications of spinal anesthesia. This review article focuses on what is new, interesting, and clinically relevant for this simple and popular technique.

Anatomy

Meninges

Many anatomic structures important for spinal anesthesia have only recently been investigated. The arachnoid membrane is a structure of obvious interest, as spinal agents must be delivered within its confines. The arachnoid membrane is composed of overlapping layers of epithelial cells connected by tight junctions.[4] This anatomic arrangement allows the arachnoid membrane, not the dura, to function as the principal meningeal barrier (90% of resistance) to materials crossing in and out of the cerebrospinal fluid (CSF).[4] A functional proof of the arachnoid's importance as gatekeeper to the CSF is that spinal CSF resides in the subarachnoid and not subdural space. The arachnoid membrane serves not only as a passive container of CSF but also actively processes and transports agents attempting to cross J1te meninges. Recent studies demonstrated that metabolic enzymes are expressed in the arachnoid that can affect agents (*e.g.*, epinephrine)[5] and neurotransmitters important for spinal anesthesia (*e.g.*, acetylcholine).[6–8] Active transport of compounds across the arachnoid membrane occurs in the area of the neural root cuffs.[8] Here, unidirectional transport of materials from the CSF into the epidural space occurs and may contribute to clearance of spinal anesthesia agents. Another potential clinical consideration of the lamellar structure of the arachnoid is easy separation of the arachnoid membrane from the dura during spinal puncture. This mechanical arrangement allows easy subdural deposition of spinal agents despite the free return of CSF during spinal injection, which may help to explain individual effects of spinal anesthesia.[9]

Spinal Cerbrospinal Fluid Volume

After injection of spinal anesthetics, dilution with the CSF occurs before arrival at effector sites in the central nervous system. Thus, individual variation in lumbosacral volumes of CSF and distribution within this volume will affect spinal anesthesia. Recent use of magnetic resonance imaging (MRI) demonstrates great variability between individuals in volume of lumbosacral CSF, with a range of 28–81 ml.[10] Interestingly, obese individuals have substantially less CSF (~10 ml less), which is partly caused by compression of the neural foramina. Clinical correlation between volume of lumbosacral CSF and spinal anesthesia with hyperbaric lidocaine and isobaric bupivacaine is excellent, with CSF accounting for 80% of the variability for peak block height and regression of sensory and motor block (fig. 1).[11] Unfortunately, volume of lumbosacral CSF does not correlate with external physical measurements other than weight ($r = 0.4$, $P < 0.05$); therefore, volume cannot be easily estimated from physical examination.[11] Other important considerations include the observation on MRI that the CSF is not a "still lake" of fluid but vigorously oscillates with arterial pulsations.[9] These wavelike movements may be another important factor in distribution and clearance of spinal agents and may influence neurotoxicity from exposure to concentrated agents (see Transient Neurologic Symptoms–Neurotoxicity).

Spinal Nerve Roots

The target sites of spinal anesthetics are the spinal nerve roots and spinal cord. In a similar fashion to volume of CSF, individual variability in anatomy of spinal nerve roots may also explain variability in spinal anesthesia.[12,13] Recent autopsy and microscopic studies have

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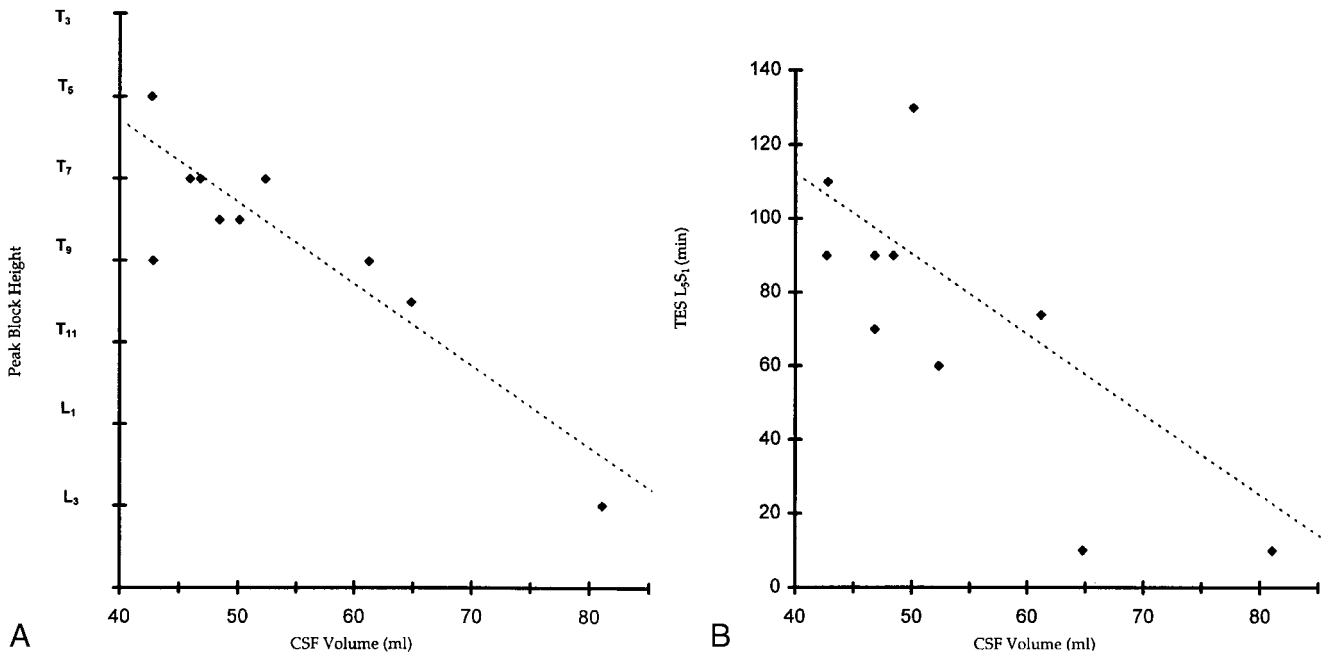

Fig. 1. (*A*) Correlation between lumbosacral cerebrospinal fluid (CSF) volume and peak sensory block height (r = 0.91, $P < 0.05$). (*B*) Correlation between lumbosacral CSF volume and duration of anesthesia to transcutaneous electrical stimulation at the ankle (TES L5–S1) which is a surrogate for duration of surgical anesthesia. R = 0.83, $P < 0.05$. (Reprinted with permission.[11])

observed great interindividual variability in size of human nerve roots. For example, the range of the posterior nerve root of L5 is 2.3–7.7 mm^3. Other interesting anatomic findings are the relatively larger size of dorsal nerve roots, compared with ventral, with packaging into easily separable strands.[13] Although a larger dorsal nerve root would seem more impenetrable to local anesthetics, the separation of the dorsal root into component bundles creates a much larger surface area for local anesthetic penetration than the single smaller ventral nerve root. This anatomic finding may help explain the relative ease of sensory *versus* motor block.

Finally, recent microscopic and endoscopic examination of the subarachnoid space reveals the presence of numerous membranes surrounding nerve roots and ligaments within the arachnoid that potentially compartmentalize spinal CSF.[9] These partitions may help to concentrate local anesthetics near nerve roots and augment spinal anesthesia but could also impede communication of CSF between dorsal and ventral nerve roots, thus again explaining relative difficulty of achieving motor block.

Physiology

Thermoregulation

Mild perioperative hypothermia is associated with an increased incidence of myocardial ischemia, cardiac morbidity, wound infection, blood loss, and transfusion requirements.[14] Both general and regional anesthesia impair temperature homeostasis to a similar degree,[15,16] and careful monitoring and active maintenance of temperature is a simple means to prevent morbidity.

The effects of spinal anesthesia on temperature homeostasis have been well studied, and there are three main mechanisms causing core hypothermia.[14,15,17,18] The first is redistribution of central heat to the periphery caused by vasodilation from sympathetic block. This effect is maximal during the first 30–60 min, causes a decrease in core temperature of approximately 1–2°C, and depends on extent of sensory block and patient age (fig. 2).[19] The second mechanism is loss of thermoregulation characterized by reduced shivering and vasoconstriction thresholds during spinal anesthesia. This abnormal tolerance for hypothermia occurs because of subjective warmth exceeding the actual surface temperature increase from sympathectomy. This exaggerated sense of warmth is proportional to extent of sensory and sympathetic block[15] and decreases thresholds for shivering and vasoconstriction. Thus, hypothermia may occur during spinal anesthesia without a conscious perception of cold.[20] Finally, with loss of thermoregulatory vasoconstriction below the level of the sympathetic block, there is increased heat loss from vasodilation. Spinal anesthesia will predictably cause core hypothermia within 30–60 min, and patients should be monitored and actively warmed if needed.[14]

Unfortunately, a recent survey of practicing members of the American Society of Anesthesiologists revealed that only 33% of practitioners use temperature monitoring during regional anesthesia.[18] Furthermore, temperature was most commonly monitored on a surface site

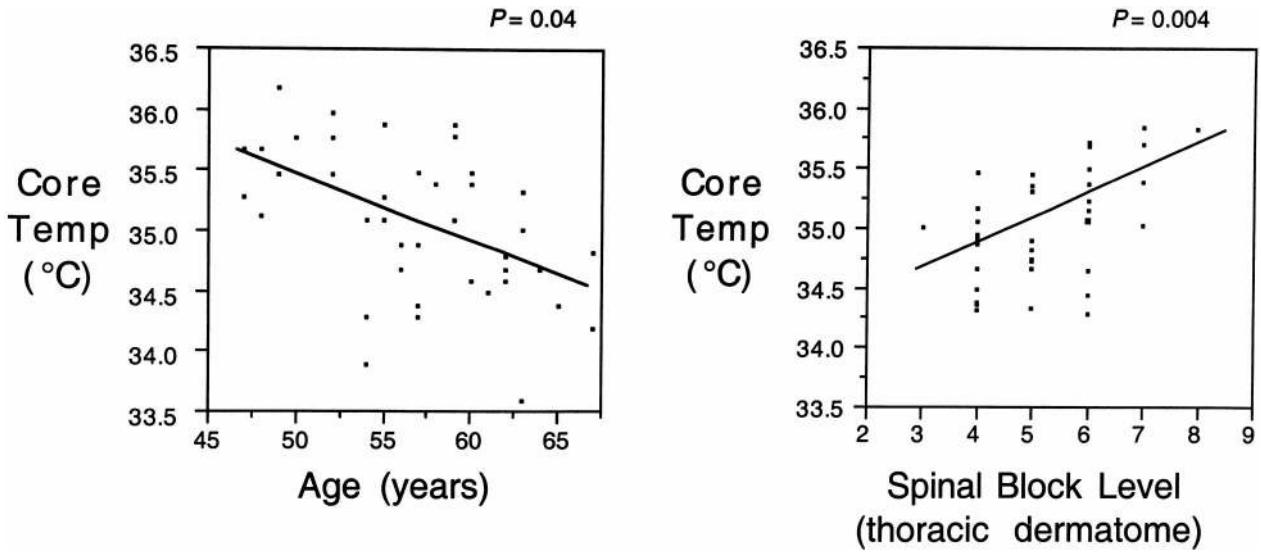

Fig. 2. Peak sensory block height to pinprick correlates with core hypothermia on admission to the postanesthesia care unit ($P < 0.004$). (Reprinted with permission.[19])

such as the forehead and not at accessible core temperature sites during regional anesthesia (*e.g.*, tympanic membrane). These surface sites provide inherently inaccurate estimates of core temperature during regional anesthesia because of the aforementioned redistribution of core heat, compensatory vasoconstriction above the level of spinal anesthesia, and influence of ambient temperature.[16] If hypothermia develops, patients should be rewarmed with forced air heating. Spinal anesthesia accelerates rewarming compared with general anesthesia because of the residual sympathetic block and vasodilation.[15]

Cardiovascular

The most common serious side effects from spinal anesthesia are hypotension and bradycardia,[21,22] and closed claims surveys of 40,000–550,000 spinal anesthetics indicate an incidence of cardiac arrest from 0.04–1/10,000.[23,24] Large surveillance studies typically observed incidences of hypotension around 33% and bradycardia around 13% in nonobstetric populations.[21,22] Risk factors for hypotension in nonobstetric populations include block height T5 or greater (odds ratio [OR], 3.8), age 40 yr or greater (OR, 2.5), baseline systolic blood pressure less than 120 mmHg (OR, 2.4), and spinal puncture above L3–L4 (OR, 1.8). Risk factors for development of bradycardia in nonobstetric populations include baseline heart rate less than 60 beats/min (OR, 4.9), American Society of Anesthesiologists physical status I (OR, 3.5), use of β blockers (OR, 2.9), prolonged PR interval on electrocardiogram (OR, 3.2), and block height T5 or greater (OR, 1.7).[21,25] Analysis of closed claims for cardiac arrest during spinal anesthesia indicated that administration of sedation to produce a sleep-like state without spontaneous verbalization and lack of early administration of epinephrine were common patterns of management in cases of cardiac arrest.[26]

Cardiovascular effects of spinal anesthesia typically include a decrease in arterial blood pressure and central venous pressure with only minor decreases in heart rate, stroke volume, or cardiac output even in patients with poor left ventricular function (ejection fraction < 50%; fig. 3).[27,28] Typical preservation of cardiac output during spinal anesthesia allows maintenance of oxygen delivery to vital organs such as the brain, as demonstrated by lack of change in jugular bulb oxygen saturation.[29] The decrease in sympathetic activity and motor block also leads to a decrease in total body oxygen consumption that correlates with extent of spinal anesthesia.[30]

Hypotension occurs from decreases in systemic vascu-

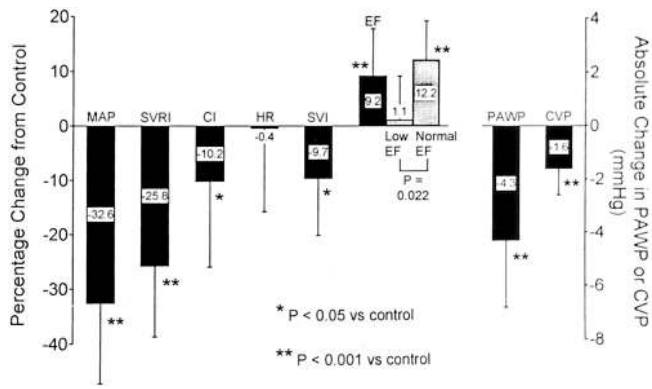

Fig. 3. The percentage of change or absolute change from baseline (± SD) in hemodynamics after spinal anesthesia in 15 elderly men with cardiac disease. MAP = mean arterial pressure; SVRI = systemic vascular resistance index; CI = cardiac index; HR = heart rate; SVI = stroke volume index; EF = left ventricular ejection fraction; PAWP = pulmonary artery wedge pressure; CVP = central venous pressure. The EF response is subdivided for the four subjects with baseline EF less than 50% (Low EF) and the 11 subjects with baseline EF 50% or greater (Normal EF). The major cause for decrease in MAP was a decrease in SVRI and not CI. The major cause for decreasing CI was decrease in SVI and not HR. (Reprinted with permission.[27])

lar resistance and central venous pressure from sympathetic block with vasodilation and redistribution of central blood volume to lower extremities and splanchnic beds.[27,28,31,32] This sympathetic block is rarely complete, and some preservation of sympathetic reflexes to stressful challenge typically occurs.[33] Sudden bradycardia can occur from shift in cardiac autonomic balance toward the parasympathetic system, as evidenced in spectral analysis of heart rate variability,[34] from activation of left ventricular mechanoreceptors from a sudden decrease in left ventricular volume (Bezold Jarisch reflex),[35] or from increases in baroreflex activity.[36]

Various prophylactic and rescue regimens have been advocated for hemodynamic disturbances with emphasis on prevention of hypotension. Studies are difficult to interpret because of different definitions of hypotension and different patient populations (elderly, pregnant, surgical).[28] Prophylactic measures include prehydration with crystalloid or colloid or administration of vasoactive agents. On the whole, prehydration of crystalloid (250–2,000 ml) appears to temporarily increase preload and cardiac output without consistently increasing arterial blood pressure or preventing hypotension.[22,32,37–40] Pharmacokinetics of crystalloid explain its poor efficacy, as crystalloid is quickly redistributed from the intravascular to the extravascular space.[41] Administration of large volumes (> 1 l) of crystalloid does not appear to confer additional benefit over small volumes (250 ml)[38] and may be detrimental to patients with limited cardiopulmonary reserve. Prehydration with colloid (≥ 500 ml) appears to be more effective than crystalloid at maintaining arterial blood pressure and perhaps decreasing incidence of hypotension depending on definition and population.[39] The greater effectiveness of colloid is a result of greater effect for increasing central venous pressure and cardiac output caused by slower redistribution out of the intravascular space (fig. 4).[41] In contrast to prophylaxis, treatment of hypotension during spinal anesthesia will be effective with crystalloid or colloid because of changes in kinetics induced by spinal anesthesia[42] and intravascular hypovolemia.[43] Both clinical scenarios alter kinetics of cystalloid and colloid to allow retention within the intravascular space.

Prophylactic administration of pharmacologic agents may be more effective than prehydration for prevention of hypotension.[44] α-Adrenergic agonists (*e.g.*, metaraminol, phenylphrine) reliably increase arterial blood pressure by increasing systemic vascular resistance; however, heart rate and cardiac output may decrease because of increased afterload.[22,32,45] Mixed α- and β-adrenergic agents (*e.g.*, ephedrine, epinephrine) are also effective for increasing arterial blood pressure and preventing hypotension but act by primarily increasing heart rate and cardiac output with a smaller increase in systemic vascular resistance.[28] These different physiologic mechanisms for α- *versus* mixed α- and β-adrenergic agents also occur in treatment of hypotension during spinal anesthesia (fig. 5).[31] Thus, initial treatment can be tailored to α only for patients with hypotension and mixed α and β for patients with both hypotension and bradycardia.

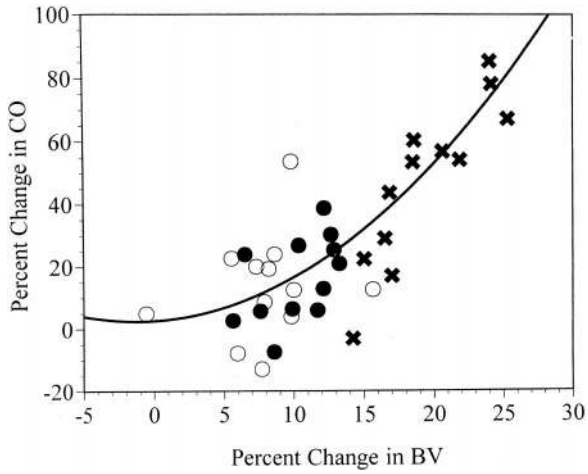

Fig. 4. Use of crystalloid and colloid for volume preloading in healthy parturients. Use of 1.5 l lactated Ringer's solution (open circles) or 0.5 l 6% hydroxyethylene starch (closed circles) produces mild increases in cardiac output (CO) and blood volume (BV), whereas preloading with 1 l 6% hydroxyethylene strach (X) produced substantial increases in CO and BV. (Reprinted with permission.[39])

A potential means for prophylaxis of hypotension is by manipulation of spinal anesthesia to achieve a predominantly unilateral block. Unilaterality can be maintained if the patient remains in a lateral position for surgery; however, eventual turning of the patient into a supine position results in partial redistribution to bilateral anesthesia.[46] Unilaterality can be maximized by using a side port spinal needle (*e.g.*, Whitacre)[47] and a small dose of local anesthetic,[48] and by keeping the patient in the lateral position for 6–20 min.[46] Concentration of anesthetic solution[49] and speed of injection[50] are minor factors for unilaterality.[51] With such optimization of unilaterality and decreased extent of sympathetic block, hypotension has been reported to decrease from 22–53 to 5–7%.[44,52]

Supraspinal Effects on Consciousness

There has been a recent convergence in mechanisms of general and spinal anesthesia. Minimum alveolar concentration, a traditional measure of inhalational agent potency for depth of anesthesia, appears to have a primary mechanism in the spinal cord.[53] In contrast, central neuraxial anesthesia may have direct effects on suppression of consciousness, and multiple studies have observed that patients appear drowsy after spinal anesthesia despite lack of sedative medications.[54,55] Correspondingly, both spinal and epidural anesthesia reduce the hypnotic requirements of midazolam, isoflurane, sevoflurane, and thiopental in surgical patients and laboratory studies.[56] Possible mechanisms for decreased consciousness during spinal an-

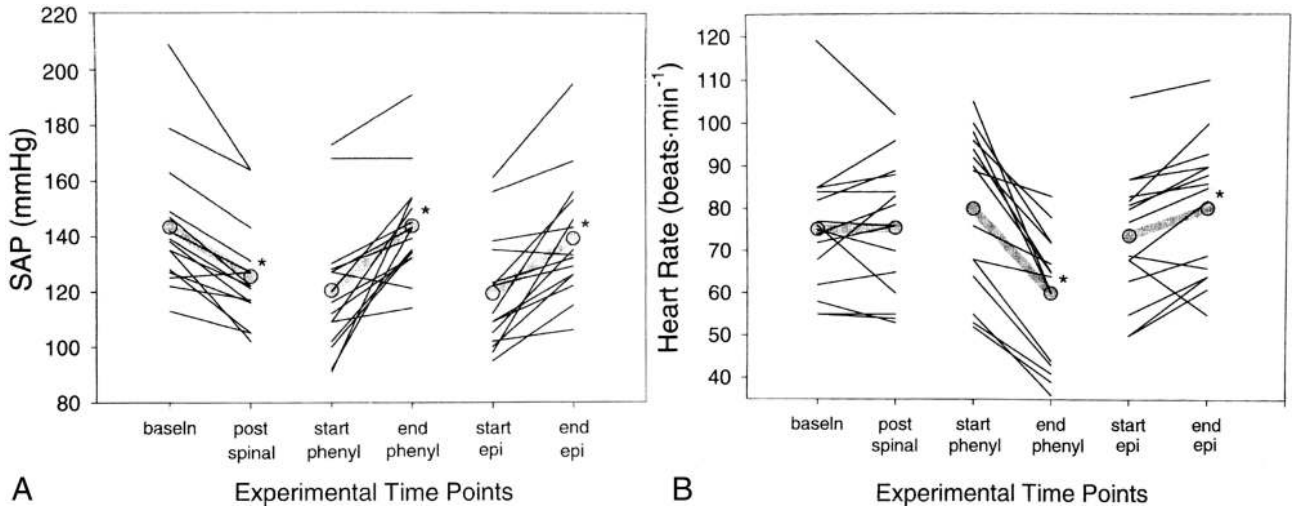

Fig. 5. Epinephrine (epi) and phenylephrine (phenyl) were infused in a randomized, blinded, crossover manner to treat hypotension after tetracaine spinal anesthesia. (*A*) Effects of spinal anesthesia and drug treatment on systolic arterial pressure (SAP). (*B*) Effects of spinal anesthesia and drug treatment on heart rate. *$P < 0.001$. (Reprinted with permission.[28])

esthesia include rostral spread of local anesthetics or decrease in reticular activating system activity caused by interruption of afferent input.[54] Animal models support the latter, as spinal anesthesia in rats decreases hypnotic requirements of thiopental without detection of local anesthetic in the brain or cervical spinal cord.[57] In humans, degree of sedation caused by spinal anesthesia is related to peak block height, with greater sedation observed with greater block heights.[58] This finding again indirectly supports the hypothesis that greater loss of afferent input from extension of spinal anesthesia increasingly suppresses consciousness. Time of maximal sedation with spinal anesthesia in volunteers shows a biphasic distribution, with one peak occurring during peak spinal block (~30 min after injection) and a second peak occurring later, approximately 1 h after injection.[54] Mechanisms for the second peak in sedation are unclear and may include late rostral spread of local anesthetic into the brain or psychological relief over regression of spinal anesthesia. Clinical relevance for these observations is the decreased need for pharmacologic sedatives with the use of spinal anesthesia.

Mechanism of Spinal Anesthesia

Injection of local anesthetics into the spinal CSF allows access to sites of action both within the spinal cord and the peripheral nerve roots.[28] The traditional concept of spinal anesthesia causing complete conduction block is simplistic, as studies with somatosensory evoked potentials demonstrate little change in amplitudes or latencies after induction of dense spinal or epidural anesthesia.[59] There are multiple potential actions of local anesthetics within the spinal cord at different sites. For example, within the dorsal and ventral horns, local anesthetics can exert sodium channel block and inhibit generation and propagation of electrical activity.[60] Other spinal cord neuronal ion channels, such as calcium channels, are also important for afferent and efferent neural activity. Spinal administration of N-type calcium channel blockers results in hyperpolarization of cell membranes, resistance to electrical stimulation from nociceptive afferents, and intense analgesia.[61] Local anesthetics may have similar actions on neural calcium channels, which may contribute to analgesic actions of central neuraxially administered local anesthetics.[62]

Multiple neurotransmitters are involved in nociceptive transmission in the dorsal horn of the spinal cord.[63] Substance P is an important neurotransmitter that modulates nociception from C fibers and is released from presynaptic terminals of dorsal root ganglion cells. Administration of local anesthetics in concentrations that occur after spinal and epidural anesthesia inhibits release of substance P and inhibits binding of substance P to its receptor in the central neuraxis in a noncompetitive fashion.[64] Other inhibitory neurotransmitters that may be important for nociceptive processing in the spinal cord, such as γ-aminobutyric acid, are also affected by local anesthetics. Local anesthetics can potentiate the effects of γ-aminobutyric acid by preventing uptake and clearance.[65] These studies suggest spinal anesthesia may be partially mediated *via* complex interactions at neural synapses in addition to ion channel blockade and may explain the ability of spinal anesthesia to reduce central temporal summation in humans.[66]

Although spinal local anesthetics can block sodium channels and electrical conduction in spinal nerve roots, other mechanisms may also come into play. It is theorized that a large part of the sensory information transmitted *via* peripheral nerves is carried *via* coding of electrical signals in after-potentials and after-oscillations.[67,68] Evidence for this theory is found in studies demonstrating loss of sensory nerve function after incomplete local anesthetic blockade. For example, sensa-

Table 1. Typical Dose–Response Effects of Spinal Local Anesthetics for Ambulatory Anesthesia

Local Anesthetic	Dose (mg)	Peak Block	Duration of Sensory Block (min)	Duration of Motor Block (min)	Time from Induction until Discharge (min)	Anesthetic Success Rate (%)
Lidocaine (isobaric)	30					0
	40	T4 (T2–T10)	130 (26)	93 (24)	178 (34)	90
	60	T3 (T2–T10)	162 (32)	128 (31)	216 (33)	90
	80	T3 (T1–T7)	170 (24)	142 (32)	236 (46)	97
Bupivacaine (hyperbaric)	5	T5 (T4–T7)	123 (27)	50 (20)	181 (30)	75
	7.5	T8 (T4–T11)	144 (25)	75 (24)	202 (28)	100
	10	T8 (T6–T10)	194 (26)	100 (24)	260 (30)	100
Mepivacaine (isobaric)	30	T9 (T2–L5)	158 (32)	116 (38)	180 (34)	72
	45	T6 (T2–T12)	182 (38)	142 (37)	191 (29)	100
	60	T5 (T2–L1)	203 (36)	168 (36)	203 (35)	100
Ropivacaine (isobaric)	8	T9 (T4–L1)	130 (27)	107 (25)	165 (45)	63
	10	T8 (T4–L2)	152 (44)	135 (31)	174 (38)	83
	12	T8 (T4–L1)	176 (42)	162 (37)	199 (52)	93
	14	T9 (T3–L1)	192 (48)	189 (44)	233 (52)	100
Procaine (hyperbaric)	100	T5 (T1–T10)	120 (23)	100 (30)	244 (43)	83
Prilocaine (hyperbaric)	50	T6 (T1–T10)	128 (38)	165 (37)	253 (55)	100

Increasing doses of spinal local anesthetics increases duration of both anesthesia and recovery. Dose response data allow selection of appropriate dose for planned anesthetic duration. Isobaric solutions are glucose-free. Hyperbaric solutions contain glucose or dextrose. Data are from references 72, 73, 84, 85, 91, and 94–96.

tion of temperature of the skin can be lost despite unimpeded conduction of small fibers.[69] Furthermore, a surgical depth of epidural and spinal anesthesia can be obtained with only minor changes in somatosensory evoked potentials from the anesthetized area.[59,70] Previous studies have demonstrated that application of subblocking concentrations of local anesthetic will suppress normally occurring after-potentials and after-oscillations without significantly affecting action potential conduction.[69] Thus, disruption of coding of electrical information by local anesthetics may be a primary mechanism for block of spinal nerve roots during spinal anesthesia.

Clinical Applications

Ambulatory Anesthesia

Introduction of small-gauge pencil-point spinal needles has reduced the risk of postdural puncture headache (PDPH) to approximately 1%,[71] and use of spinal anesthesia for ambulatory surgery has become more popular. The ideal spinal anesthetic would combine rapid and adequate surgical anesthesia with rapid achievement of discharge criteria such as ambulation and urination. The most important determinant of both successful surgical anesthesia and time until recovery is dose of local anesthetic.[72,73] Neither volume of injectate nor concentration of solution within a 10-fold range (0.5–5% lidocaine) have significant effects.[74,75] Unfortunately, selection of dose for ambulatory spinal anesthesia will inherently result in variable individual patient response. Both pharmacokinetics and pharmacodymanics of individual patients are highly variable and are not easily predicted by individual patient demographics (*e.g.*, age, height).[76] However, ambulatory spinal anesthesia can be designed to provide similar discharge times (~202 min) as general anesthesia (~185 min).[77] Further acceleration of patient discharge may or may not improve efficiency depending on institutional staffing, compensation of staff, and patient volume.[78]

Determination of appropriate patient discharge criteria for ambulatory anesthesia and surgery are evolving.[79] Ability to void is a common discharge criterion that may delay patient discharge after resolution of spinal anesthesia.[79,80] Recent evidence suggests that patients at low risk (*e.g.*, nonpelvic surgery, no history of urinary retention) for urinary retention do not need to void before being discharged home.[79,81,82] High-risk patients may be monitored and managed optimally by bladder ultrasound determination of urine volume and need for catheterization.[82,83]

Local Anesthetics.

Lidocaine. Spinal lidocaine has been a popular choice for ambulatory spinal anesthesia, and recent studies have examined dose–response effects of lidocaine on anesthesia and recovery (table 1).[84,85] Although lidocaine has enjoyed a long history of safety and popularity since its introduction in 1945, it has come under recent scrutiny because of transient neurologic symptoms (TNS). TNS is clearly associated with use of spinal lidocaine, with an approximate incidence of 20% in the ambulatory setting (table 2).[86–88] Concern over the potential for neurologic injury and for patient comfort has led to interest in alternative spinal local anesthetics. An ideal replacement for lidocaine should posses clinical characteristics suitable for ambulatory anesthesia (fast, successful anesthesia with rapid recovery) and less risk for TNS.

Bupivacaine. Bupivacaine has been the most studied alternative to lidocaine. TNS is virtually absent in all clinical studies with spinal bupivacaine (0–1%; table

Table 2. Typical Incidences of TNS with Outpatient Spinal Anesthesia

Local Anesthetic	Patient Position	TNS (%)
Lidocaine 2–5%	Supine	6
Lidocaine 3%	Prone	0.4
Lidocaine 0.5%	Knee arthroscopy	17
Lidocaine 5%	Knee arthroscopy	16
Lidocaine 5%	Lithotomy	24
Bupivacaine 0.25–0.75%	Supine	0–1
	Knee arthroscopy	0–1
	Lithotomy	0–1
Mepivacaine 1.5%	Knee arthroscopy	8
Mepivacaine 4%	Mixed	30
Ropivacaine 0.25%	Supine	1
Ropivacaine 0.2–0.35%	Knee arthroscopy	0
Procaine 5%	Knee arthroscopy	6
Prilocaine 2–5%	Mixed	3–4

Bupivacaine and ropivacaine consistently result in low incidences of transient neurologic symptoms (TNS), whereas lidocaine typically results in the highest incidences. Other local anesthetics are intermediate in incidence of TNS. Data are from references 63, 86, 92, 96, and 99.

2).[86–88] Recent dose–response data on clinical anesthetic characteristics for spinal bupivacaine (table 1) indicate that small doses can be used for ambulatory anesthesia.[72,89] It is particularly important to select small doses of bupivacaine ($\leq$ 10 mg) to avoid prolonged detrusor block, inability to void, and excessively prolonged time until discharge as compared with equipotent doses of lidocaine.[80]

Mepivacaine. Mepivacaine has been used for spinal anesthesia since the 1960s. Clinical anesthetic characteristics are similar to lidocaine, with an approximate potency of 1.3:1 (table 1).[90,91] Reported risk of TNS with mepivacaine is highly variable. Small-scale studies (60–75 patients) report a low incidence of TNS (0–8%), whereas larger studies (200+ patients) report incidences of approximately 30% (table 2).[90,92] It seems mepivacaine has similar clinical characteristics as lidocaine for spinal anesthesia but likely shares the same risk of TNS.

Ropivacaine. Ropivacaine is a new local anesthetic released in the United States in 1996. It is a lipid-soluble agent that is approximately 50–60% as potent as spinal bupivacaine. Like bupivacaine, there is little risk of TNS with use of spinal ropivacaine (0–1% incidence; table 2).[93,94] The decreased potency of ropivacaine offers the potential for more rapid recovery and better suitability as an outpatient spinal anesthetic. However, dose–response data indicate that equipotent doses of ropivacaine will have similar recovery times as bupivacaine (table 1).[93,94] Thus, ropivacaine in equipotent doses (2:1) will be virtually indistinguishable from bupivacaine for clinical anesthesia and risk of TNS without any obvious advantages.

Procaine. Procaine was the first synthesized local anesthetic and has been used for spinal anesthesia since the early 1900s. Procaine has suitable clinical characteristics for brief spinal anesthesia but was supplanted by lidocaine because of more reliable anesthesia and fewer side effects. For unclear reasons, procaine carries a higher risk of nausea than other spinal local anesthetics (OR, 3:1).[21] No studies have adequately determined dose–response data[95] for spinal procaine, and very few have compared it with lidocaine. A recent prospective, randomized, double-blind study compared 100 mg hyperbaric procaine to 50 mg hyperbaric lidocaine (2:1 ratio) for ambulatory knee arthroscopy.[96] This study observed a higher anesthetic failure rate with the procaine (17% *vs.* 3%), a higher incidence of nausea (17% *vs.* 3%), and a 30-min longer time until readiness for discharge. Although a larger dose of procaine would probably increase anesthetic success, a larger dose would likely further increase the greater risk of nausea and prolonged recovery. The risk of TNS was much less with procaine *versus* lidocaine (6% *vs.* 24%). Thus, recent data on procaine spinal anesthesia are not encouraging, as it appears to be less reliable for surgical anesthesia than lidocaine while having a slower recovery (table 1). Risk of TNS is less than lidocaine but probably greater than bupivacaine (table 2).

Prilocaine. Prilocaine is unavailable in the United States for central neuraxial use. It is an amide local anesthetic with pharmacologic properties similar to lidocaine. There are no dose–response data with prilocaine to allow determination of optimal doses for ambulatory spinal anesthesia, nor are there formal potencies to allow comparison with lidocaine. Recent studies suggest that prilocaine is approximately equipotent to lidocaine within a dose range of 40–70 mg[87,97] and thus may have suitable clinical characteristics for ambulatory spinal anesthesia (table 1). Risk of TNS appears to be minimal with spinal prilocaine (0–1%; table 2).[87,97] Prilocaine could be a suitable agent for ambulatory spinal anesthesia with fast recovery properties and low risk of TNS.

Analgesic Additives. Both anesthetic success and especially time until readiness for discharge are dependent on dose of local anesthetic. There has been recent interest in using analgesic additives to spinal local anesthetics to decrease the dose of local anesthetic for faster recovery while maintaining or improving anesthetic success. The optimal analgesic additive would increase anesthetic success while sparing local anesthetic and decreasing time until discharge. Multiple analgesics are active in the spinal cord and could potentially be used as spinal anesthesia additives.[63] However, analgesic activity (dose response, effects on acute *vs.* chronic pain) and neurotoxicity have not been fully evaluated for the multitude of known analgesics. Thus, only reasonably well-investigated agents are discussed in the following sections (table 3).

Vasoconstrictors. Both epinephrine and phenlyephrine have a long history as additives to local anesthetics. Both agents will intensify and prolong sensory and mo-

Table 3. Intrathecal Spinal Analgesic Additives for Ambulatory Anesthesia

Agent	Dose	Typical Anesthetic Effect	Typical Effect on Anesthetic Recovery
Fentanyl	10–25 μg	25% Increase in duration of surgical anesthesia 33% Increase in anesthetic success with small doses of local anesthetic 60% Incidence of easily treated pruritus	None
Clonidine	200 μg oral 15–45 μg	30% Increase in duration of surgical anesthesia 29% Increase in duration of motor block 37% Increase in anesthetic success with small doses of local anesthetic Mild perioperative sedation and decrease in heart rate and blood pressure	None
Epinephrine	0.1–0.6 mg	Dose-related increase in surgical anesthesia and motor block	Dose-related increase in time until recovery of the same or greater magnitude
Neostigmine	6.25–50 μg	Dose-related increase in surgical anesthesia and motor block Dose-related increase in nausea and vomiting	Dose-related increase in time until recovery of the same or greater magnitude

Data are from references 98–102, 104–106, 111, 116, and 118–120.

tor anesthesia[98–100] and allow use of lower doses of local anesthetic in a dose-dependent fashion (0.1–0.6 mg).[101] Vasoconstrictors may act by a combination of decreased clearance of spinal local anesthetic *via* vasoconstriction and direct analgesic effects on spinal cord α-adrenergic receptors. Unfortunately, their usefulness for ambulatory spinal anesthesia is limited by their propensity to prolong recovery from sensory and motor block and ability to urinate to a disproportionate degree as compared with anesthetic benefit (table 3).[100] For example, addition of 0.2 mg epinephrine to 60 mg 2% isobaric lidocaine in patients undergoing outpatient knee arthroscopy prolonged sensory block by 90 min but prolonged recovery milestones and time to discharge by 106 min.[102] Similar effects are observed with bupivacaine[98] and procaine.[95] Use of epinephrine is not associated with increased risk of TNS[88] but has been associated with a case report of cauda equina syndrome.[103] Use of phenylephrine has been implicated as a risk for TNS (10-fold increase).[99] Thus, use of vasoconstrictors are safe and effective for prolonging and intensifying spinal anesthesia but are ill advised for ambulatory surgery because of delay in patient recovery and potential increased risk of TNS.

Opioids. Opioids were the first clinically used selective spinal analgesics after the discovery of opioid receptors in the spinal cord.[104] Intrathecal opioids selectively decrease nociceptive afferent input from Aδ and C fibers without affecting dorsal root axons or somatosensory evoked potentials.[104] Hydrophilic opioids such as morphine provide excellent selective spinal analgesia because of small volume of distribution and slow clearance from the spinal cord.[8] However, slow spinal cord penetration and prolonged duration in CSF caused by hydrophilicity also results in slow onset (> 30 min), prolonged duration of action (6+ h), and risk of delayed respiratory depression from rostral spread in CSF. Lipophilic opioids have a more favorable clinical profile of fast onset (minutes), modest duration (1–4 h), and little risk of delayed respiratory depression.[104] Fentanyl and sufentanil are the most commonly used spinal lipophilic opioids. Clinical studies suggest that intrathecal administration of sufentanil may produce selective spinal analgesia; however, laboratory studies suggest that systemic uptake followed by supraspinal analgesia may be the dominant mechanism of action. Because of the extreme lipid solubility of sufentanil, it has a very large volume of distribution in the spinal cord with rapid clearance into the spinal cord vasculature and epidural space in pig models.[8] This laboratory finding implies that very little spinal sufentanil is available for interaction with spinal cord opioid receptors because of sequestration in lipid soluble white matter and systemic redistribution. Further studies are needed to determine the dominant mechanism of action of spinal sufentanil and whether spinal administration is rational.

Fentanyl is less lipid soluble and will maintain modest spinal selectivity when injected intrathecally.[7,8] Dose–response data indicate that spinal fentanyl alone provides dose-dependent analgesia with a minimally effective dose of approximately 10 μg.[105] Risk of early respiratory depression is also dose-dependent, with significant risk occurring with doses greater than 25 μg (fig. 6).[106] Addition of fentanyl to spinal anesthesia produces synergistic analgesia for somatic and visceral pain without increased sympathetic block.[104] In addition, mixture of fentanyl with local anesthetic solution decreases baricity and may alter distribution of agents in CSF.[107] Taken as a whole, the best risk–benefit dose range would be addition of 10–25 μg fentanyl. Side effects will be limited to easily treated pruritus (~ 60%),[108,109] while risk of early respiratory depression and urinary retention will be minimized.[106,108,110]

Numerous clinical studies have demonstrated that addition of 10–25 μg fentanyl improves success of spinal

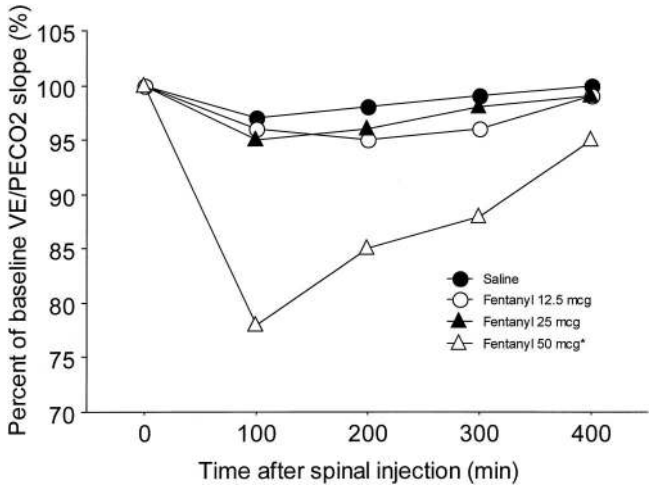

Fig. 6. Effects of spinal lidocaine with and without spinal fentanyl on ventilatory response to carbon dioxide (V_E/P_{ECO_2}). The 50-μg dose of spinal fentanyl produced significant respiratory depression. *$P < 0.05$. (Data from Varrassi *et al.*[106])

anesthesia, allows use of less local anesthetic, and does not prolong duration until discharge (table 3). For example, 10 μg fentanyl added to 5 mg hyperbaric bupivacaine for outpatient knee arthroscopy improved anesthetic success from 75% with plain bupivacaine to 100%.[111] A dose of 7.5 mg plain bupivacaine is needed to achieve similar success, with resultant prolongation of time until discharge of 187–202 min when compared with 5 mg plus fentanyl. Similar findings have been observed with addition of 10–25 μg fentanyl to spinal lidocaine in patients undergoing ambulatory laparoscopy and *in vitro* fertilization, and in volunteers.[108,109,112]

α₂-Adrenergic Agonists. Clonidine is the best characterized α_2-adrenergic agonist and provides dose-dependent analgesia and side effects of hypotension, bradycardia, and sedation.[113] It is not associated with side effects of spinal opioids such as respiratory depression and pruritus[113] and has less potential for causing urinary retention than spinal opioids.[114] Clonidine attenuates nociceptive input from Aδ and C fibers and acts synergistically with spinal local anesthetics.[115] Addition of either oral or spinal clonidine to spinal local anesthetics increases sensory and motor block. Oral clonidine is well absorbed with virtually 100% bioavailability and may be a useful premedication for sedation, sympathetic attenuation, and augmentation of ambulatory spinal anesthesia.[116,117] Dose- and time–response studies indicate that 150–200 μg oral clonidine administered 1–3 h before spinal anesthesia can augment sensory and motor block without delaying achievement of discharge criteria (table 3).[116] Dose–response data for spinal clonidine suggests that a dose of 15–45 μg is an optimal dose for low-dose outpatient spinal anesthesia. This dose improved anesthetic success of 8 mg ropivacaine from 60 to 100% for ambulatory knee arthroscopy without prolonging recovery (table 3).[118]

Acetylcholinesterase Inhibitors. Spinal administration of acetylcholinesterase inhibitors, such as neostigmine, inhibits breakdown of an endogenous spinal neurotransmitter (acetylcholine) that induces analgesia.[115] Release of acetylcholine in the spinal cord is stimulated by pain, systemic opioids, and spinal α_2 agonists.[115] Further analgesic effects of acetylcholine may involve stimulation of production of nitric oxide, as increased levels of spinal cord nitrite are observed after spinal administration of acetylcholine.[115] In preliminary dose–response studies conducted in volunteers and surgical patients, intrathecal neostigmine provided analgesia in doses more than or equal to 10 μg (surgical patients) to more than or equal to 50 μg (volunteers).[119] Larger doses of neostigmine caused nausea (≥100 μg) and lower extremity weakness (> 150 μg),[120] but even very large doses (750 μg) did not cause sedation, pruritus, respiratory depression, or hemodynamic depression.[119] In fact, spinal neostigmine increases activity of sympathetic neurons, counteracts the sympatholytic effects of spinal anesthesia,[121] and prevents hypotension during spinal anesthesia in animals,[122] although effects on humans with spinal anesthesia are unclear.[123] These preliminary studies suggest that small doses of neostigmine (≤ 50 μg) could enhance sensory anesthesia with few side effects when added to low-dose spinal anesthesia.

Dose–response effects of neostigmine (6.25, 12.5, and 50 μg) as an additive to low-dose (7.5 mg) bupivacaine spinal anesthesia appropriate for ambulatory anesthesia have been recently examined.[119] Addition of 50 μg neostigmine significantly improved sensory and motor block but also led to delay in achievement of discharge criteria and to a high incidence of nausea and vomiting (> 50%). Addition of even the smallest dose of neostigmine (6.25 μg) produced a high incidence of nausea and vomiting (33%) that was severe, repetitive, prolonged (2–6 h), and resistant to pharmacologic therapy. Previous studies have reported similar difficulty in preventing or treating nausea and vomiting with spinal neostigmine.[119,124] Taken as a whole, the high incidence of nausea and vomiting and prolongation of recovery from spinal anesthesia suggest that neostigmine may not be a useful additive for ambulatory spinal anesthesia (table 3).

Combined Spinal–Epidural Anesthesia

Combined spinal–epidural anesthesia (CSEA) has become an increasingly popular technique, with its estimated use increasing 10-fold between 1992 and 1997.[125] Its advantages include rapid onset, profound neuraxial block, the ability to titrate or prolong blockade, and lower total drug dosage. Possible disadvantages include increased failure rate of the spinal anesthetic, intrathecal migration of epidural drug and/or catheter, and decreased ability and reliability of epidural test dosing. Various techniques and clinical applications have been

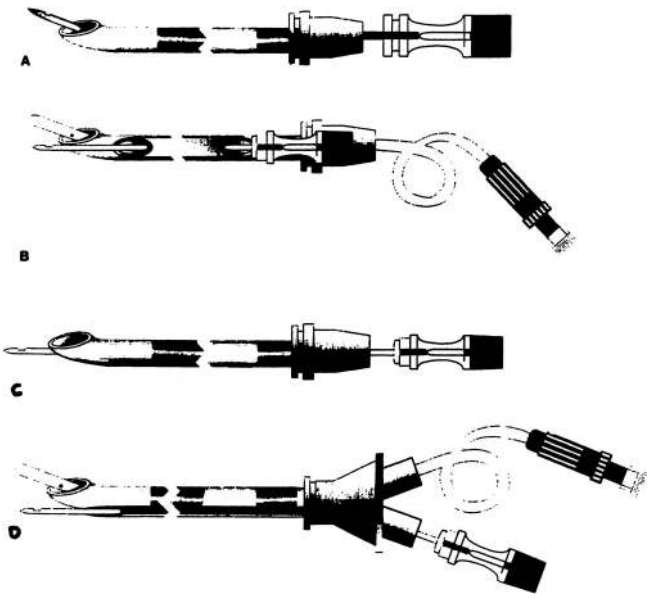

Fig. 7. Various configurations of combined spinal–epidural needles. (*A*) Needle-through-needle technique. (*B*) Eldor "double-barrel" needle. (*C*) Hanaoka "back-eye" needle. (*D*) Coombs needle. (Reprinted with permission.[127])

described, and technology has provided multiple needle configurations.

Techniques and Equipment. The most widespread approach used in the literature is the needle-through-needle technique. A number of commercial kits are available. The simplest version is a Tuohy needle (or equivalent) through which a long, small-gauge spinal needle (24–30-gauge) is passed. An epidural needle with a "back-eye" is also available, configured to reduce the risk of threading the epidural catheter through the dural hole. Some investigators suggest that the "back-eye" may result in a lower failure rate by providing a better "feel" for dural puncture.[126] Eldor[127] designed a double-barrel epidural needle with a separate conduit for the spinal needle with intended reduction of the risk of toxicity from metal fragments caused by needle friction (fig. 7). Metal fragments have been proposed as a cause of aseptic meningitis after the observation of notches in epidural needle tips.[128] However, recent evaluations using atomic absorption spectrography and photomicrography did not demonstrate metal fragments even after up to five spinal needle passes, and suggested the notches were a result of malleability of the metal.[129] One advantage to this double-barrel needle is the ability to perform the spinal anesthetic after the epidural catheter has been placed and tested.

As an alternative to the needle-through-needle technique, the double-segment method also offers the ability to place the epidural catheter and administer a test dose before placing the spinal block. Typically, the epidural and spinal portions are performed at different interspaces. By first introducing the catheter, there exists the potential risk of damaging the catheter with the spinal needle. Furthermore, creating two separate cutaneous punctures could lead to increased incidence of adverse events, including backache, headache, infection, and hematoma.[130] A recent study demonstrated greater acceptance by surgical patients of the needle-through-needle over double-segment technique(85% *vs.* 67%).[131] That same study also showed a significantly longer time to perform the double-segment technique without decreasing the failure rate of spinal anesthesia, thus suggesting that a needle-through-needle technique may be superior to a double-segment technique.

Clinical Applications.

Obstetrics. Combined spinal–epidural anesthesia has been most widely accepted in the obstetric population. The concept of the "walking epidural" has become popular among patients, where intrathecal opioid allows rapid onset of analgesia without motor blockade. Lipid-soluble opioids, such as fentanyl (up to 25 μg) and sufentanil (up to 10 μg), are most commonly used to provide 60–90 min of analgesia.[132] Adjuncts in small doses can be added to prolong the analgesic duration. For example, 2.5 mg bupivacaine can provide an additional 30 min of analgesia, as can 200 μg of epinephrine or 50 μg of clonidine.[132] A number of studies suggest that CSEA may have advantages in labor analgesia over conventional epidural analgesia. Use of CSEA may reduce incidence of instrumental vaginal delivery,[133] lower anxiety with CSEA block placement,[134] and decrease incidence of PDPH rate, possibly a result of the pressure effect of epidural administration.[135] Incidence of pruritis is significantly higher, however, in those receiving intrathecal opioids.[135]

As an anesthetic for Caesarean section, CSEA offers a rapid, titratable block with good muscle relaxation. Recently, Davies *et al.*[134] demonstrated that, compared with lidocaine–fentanyl epidural anesthesia, CSEA with 12.5 mg hyperbaric bupivacaine plus 10 μg fentanyl provided more rapid onset, better motor block, decreased anxiety levels, decreased shivering, and greater patient satisfaction. Although more ephedrine was given to the CSEA patients, the severity of hypotension did not differ, nor did the incidence of PDPHs, backaches, nausea, or vomiting.[134]

Ambulatory Anesthesia. As previously discussed, dose of local anesthetic determines both anesthetic success and duration of recovery. Availability of the epidural catheter for a rescue anesthetic allows use of marginal doses of spinal local anesthetic with resultant rapid recovery and discharge (table 1) and represents an alternative or complimentary strategy to use of analgesic additives. However, induction of a CSEA technique probably takes more time than conventional spinal anesthesia, and no current data are available to assess relative cost benefit of increased induction time *versus* decreased recovery time with CSEA.

Potential Complications.

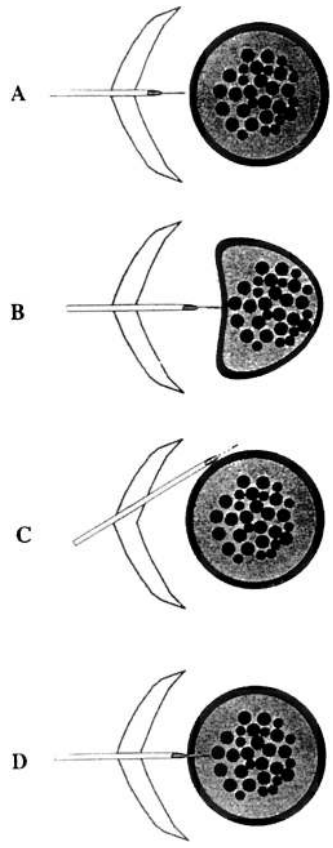

Fig. 8. Various possibilities for combined spinal–epidural block failure caused by incorrect technique. (*A*) Length of spinal needle is too short or epidural needle is not far enough into the epidural space. (*B*) Spinal needle "tents" the dura without puncture (possibly greater risk with pencil-point needles). (*C*) Epidural needle deviated from midline. (*D*) Correct technique with successful dural puncture. (Reprinted with permission.[130])

Failure of Spinal Anesthesia. The combined technique has been associated with a higher failure rate of spinal anesthesia than conventional spinal anesthesia. Most recent data suggest an approximate 5% incidence, improved from previous reports of 10–25%.[125] There are a number of reasons for failure to occur: (1) Smaller gauge spinal needles with long lengths are typically used. These needles lead to slower return of CSF and a greater resistance to injection. (2) Because the epidural needle has penetrated the tissue planes, there is little to anchor the spinal needle in place. A Luer lock apparatus is available; however, it locks at a fixed needle length and can result in not reaching or traversing the dura.[136] (3) Any deviation from midline can lead to missing the dura altogether (fig. 8). (4) If loss of resistance technique used saline, a false return of saline in the spinal needle rather than CSF can occur. Kopacz and Bainton[137] recommended the hanging drop method within the epidural needle to aide identification of dural puncture in this situation. Negative pressure from tenting the dura with the spinal needle will cause an inward movement of the drop of fluid followed by return of CSF. (5) Finally, patient positioning and duration between spinal injection and completion of epidural catheter placement can change the characteristics of the spinal block.

Failure of Epidural Anesthesia. There are no controlled randomized prospective studies addressing the failure of epidural anesthesia or analgesia with the combined technique.[138] The incidence of failure is not likely to be higher with the combined technique; however, the difficulty in early testing with a needle-through-needle technique may lead to late recognition of a misplaced catheter. Previous injection of spinal anesthetic precludes testing the epidural catheter for intrathecal placement, and epidural injection of a test dose can lead to increased height of spinal block (see below).[139] Reliability of detecting an intravascular test dose using 15 μg epinephrine remains intact in healthy individuals using heart rate and systolic blood pressure criteria, although the magnitude of hemodynamic response may be reduced.[140]

Intrathecal Effects of Epidural Agent. The intrathecal effects of epidurally administered drugs can occur through migration of the epidural catheter through the dural puncture, leakage of epidural anesthetic through the dural hole, and pressure effects of epidural injection. The likelihood of passing an epidural catheter through a dural hole is very small, provided a 24-gauge or smaller spinal needle is used. This has been demonstrated using *in vitro* models and *in vivo* epiduroscopy.[129] However, intrathecal catheter placement is possible if the epidural needle (17–18-gauge) initially rented the dura. Migration later in the anesthetic course is no more likely than with conventional epidural techniques.

Significant clinical effects of leakage of epidural local anesthetic or opioid through the small gauge dural puncture is unlikely.[129,139,141] However, significant leakage of epidural agents can occur through large dural rents such as with a "wet tap."[142,143] Pressure effect is the observation that increasing epidural volume can "squeeze" the CSF compartment and thus raise the cephalad spread of spinal drugs. A recent myelographic evaluation demonstrated that the diameter of the subarachnoid space decreased to 25% after 10 ml normal saline was injected through an epidural catheter.[144] The ability to increase dermatomal spread by epidural volume appears to be time-dependent. Sensory block extension can be significant (3–4 dermatomes) if epidural saline is injected 5–20 min after bupivacaine spinal anesthesia.[139,145] However, if delayed until two-segment regression has begun, there is no increase in sensory blockade level; in fact, it can even result in shorter duration of anesthesia.[146]

Continuous Spinal Anesthesia

The continuous spinal anesthetic (CSA) technique is regaining acceptance in the anesthesia community. Because of reports of cauda equina syndrome and lack of local anesthetic "indicated use" labels, the Food and Drug Administration withdrew the 501 K designation of

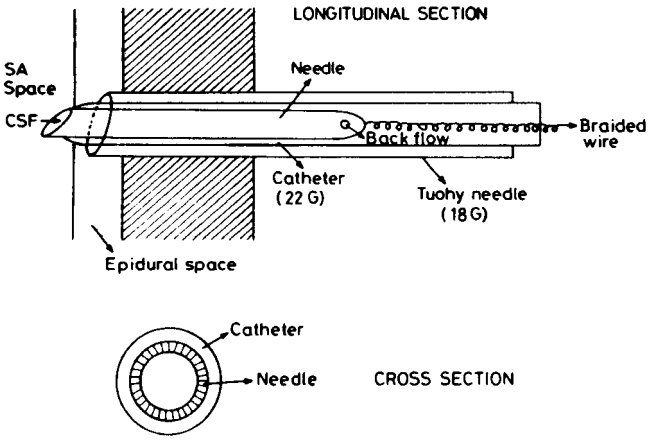

Fig. 9. Diagrammatic representation of the Spinocath in (*A*) longitudinal section and (*B*) cross-section views. SA = subarachnoid; CSF = cerebrospinal fluid. (Reprinted with permission.[148])

intrathecal microcatheters (< 24 gauge) as equivalent to approved epidural catheters in 1992. Many misinterpreted this withdrawal of exemption as confirmation that the technique was unsafe. These microcatheters were associated with potential maldistribution of local anesthetic resulting in subsequent excessive sacral dosing of local anesthetic in attempt to achieve the desired block levels. Recent reports have aimed to recognize and minimize this scenario.

Techniques and Equipment. Various needle and catheter designs are available for CSA. Microcatheters, although not available in the United States, are still widely used abroad. Adopting epidural needles and catheters for CSA is a simple and effective way of placing larger-bore macrocatheters (18–22-gauge). Newer kits, such as the Spinocath (B. Braun, Melsungen, Germany), provide an over-the-needle method in which the smaller-gauge spinal needle acts as a guide from within the larger-gauge catheter (fig. 9). This needle was designed to reduce the risk of PDPH by not promoting CSF leakage around the spinal catheter. Several studies have shown the over-the-needle systems to be technically easy to perform and efficacious, with low incidence of PDPH (0–3%).[147,148]

Clinical Applications. One of the advantages to CSA *versus* conventional spinal anesthesia is the ability to titrate local anesthetic doses. This slow titration is particularly beneficial in the hemodynamically compromised patient, such as in the elderly or in those with valvular heart disease or trauma.[149–151] A number of clinical studies have compared CSA with conventional spinal anesthesia, demonstrating fewer episodes of hypotension and lesser need for vasopressors with CSA.[151–153] Another advantage to CSA is the ability to prolong the anesthesia for long surgical cases or even for postoperative analgesia.[154] The ability to use lower anesthetic doses can lead to faster recovery times, and thus CSA may have applicability to the ambulatory setting, especially in the elderly who are less prone to PDPH.[152]

Potential Complications. A widely accepted mechanism for cauda equina syndrome and other neurologic complications associated with CSA is maldistribution of large doses of local anesthetics.[155] Caudad direction of the catheter leads to increased sacral pooling of local anesthetics and may result in neurotoxic concentrations in a small area.[156,157] The actual incidence of neurologic sequelae attributed to CSA is unknown, given small sample sizes and retrospective methods. Reports have ranged from 0.1[158,159] to 0.66%.[160] Recommendations have been made to help minimize complications: (1) in cases of poor block distribution, change baricity or patient positioning instead of adding more and more local anesthetic; (2) consider placing patients in 5–10° Trendelenberg position to decrease sacral pooling[161]; and (3) limiting the length of catheter insertion to 2 cm into the intrathecal space to avoid catheter misdirection.[162,163]

Whether the placement of an intrathecal catheter reduces the incidence of PDPH is still being debated. Earlier reports theorized that the presence of the catheter through the dural puncture site caused local inflammation and thus decreased CSF leakage.[164] Anecdotally, this lower incidence of PDPH has been demonstrated in the obstetric population, especially in patients who received an accidental dural puncture with an epidural needle.[164–166] In the surgical population, this reduction has not been demonstrated in randomized prospective studies when compared with conventional spinal anesthesia.[167,168] One retrospective study reported a PDPH incidence as high as 33.1% with microcatheters (*vs.* 3.4% with macrocatheters).[160]

Another concern is the risk of infection. Although rarely reported, concerns about infection are warranted, especially with an indwelling catheter used for postoperative or obstetric analgesia or chronic pain relief. Aseptic meningitis has been reported, but its direct association with the catheter (*vs.* contamination) is undeterminable.[160,169] One study that cultured all intrathecal catheters used postoperatively showed that bacterial colonization correlated with duration of catheter placement, and the investigators recommended limiting their use to 96 h or less.[170]

Complications of Spinal Anesthesia

Neurotoxicity of Local Anesthetics–Transient Neurologic Symptoms

The 100-year history of spinal anesthesia in humans has typically involved self-experimentation followed by widespread application, with little or no controlled testing for neurotoxicity.[1] Recent interest in neurotoxicity has arisen because of concerns over reports of cauda equina syndrome and TNS from spinal local anesthetics.

Table 4. Neurologic Complications after Spinal Anesthesia

Author	Year	Type of Study	Patients	Complications
Auroy	1997	Prospective	40,640	7 Radiculopathy 5 Cauda equina syndrome
Horlocker	1997	Retrospective	4,767	6 Persistent paresthesia
Aromaa	1997	Closed claims	550,000	5 Paraplegia 1 Cauda equina syndrome 6 Radiculopathy
Dahlgren	1995	Pro- and retrospective	8,501	4 Radiculopathy
Phillips	1969	Prospective	10,440	30 Transient paresthesia 2 Paresis 2 Exacerbation of disc disease
Moore	1969	Retrospective	11,574	1 Paresis
Sadove	1961	Retrospective	20,000	3 Meningitis 1 Paraplegia (spinal tumor)
Dripps	1954	Prospective	10,098	71 Persistent paresthesia < 1 yr 2 Foot drop 11 Neurologic exacerbation

Data are from references 63 and 176.

Animal Data. In 1985, Ready *et al.*[171] evaluated the neurotoxic effects of single injections of local anesthetics in rabbits. This group reported that spinal cord histopathology and persistent neurologic deficits were not seen with clinically used concentrations of tetracaine, lidocaine, bupivacaine, or chloroprocaine. However, histopathologic changes and neurologic deficits did occur with higher concentrations of tetracaine (1%) and lidocaine (8%). Direct effects of most local anesthetics on spinal cord blood flow are minor. Spinal administration of bupivacaine, lidocaine, mepivacaine, and tetracaine cause vasodilation and increased spinal cord blood flow, whereas ropivacaine causes vasoconstriction and reduction in spinal cord blood flow in a concentration-dependent fashion.[172] Recent studies using magnetic resonance microscopy of the spinal cord in intact rats confirm that intrathecal 5% lidocaine does not induce spinal cord ischemia.[173]

Recent studies have used desheathed peripheral nerve models designed to mimic spinal nerve roots to assess electrophysiologic neurotoxicity of clinically relevant concentrations of local anesthetics.[174] These models demonstrated that clinically used concentrations of 5% lidocaine and 0.5% tetracaine caused irreversible conduction block. Electrophysiologic toxicity of lidocaine in these models is both time- and concentration-dependent beginning at 40 mm (approximately 1%), with irreversible ablation of the compound action potential at 80 mM (approximately 2%).[63] Effects of lidocaine on peripheral nerve blood flow are also concerning, as application of 1 and 2% lidocaine with and without epinephrine to isolated rat sciatic nerve significantly depressed nerve blood flow assessed with laser Doppler flowmetry.[63]

Human Data. Despite the knowledge that all local anesthetics have the potential for neurotoxicity in the laboratory model, large-scale surveys of the complications of spinal anesthesia attest to the relative safety of spinal local anesthetics (table 4). Recent retrospective, prospective, and closed claims studies report an incidence of postoperative neurologic injury in patients undergoing spinal anesthesia between 0 and 0.7%.[23,24,63,175,176] These results include patients with preexisting neurologic conditions, including diabetes, as well as patients who experience paresthesias during spinal placement. Thus, concerns about the neurotoxic potential of spinally administered local anesthetics have not been manifest in large-scale studies to date.

There are few nonepidemiologic clinical studies evaluating the potential neurotoxicity of local anesthetics, and all have focused on electrophysiologic parameters after spinal anesthesia. Somatosensory evoked potentials, monosynaptic H-reflex, and cutaneous current perception thresholds have been used to evaluate recovery after spinal anesthesia. These measurements have shown complete return to baseline activity after 5% lidocaine spinal anesthesia in very small study populations.[177] Histopathologic or other physiologic data in humans is lacking, and thus information from controlled studies in humans is essentially not available.

Transient Neurologic Symptoms

The term TNS is used to describe symptoms of backache with radiation into the buttocks or lower extremities. This syndrome is rarely seen after general anesthesia[178] and has been described after spinal anesthesia with all local anesthetics, but most commonly with lidocaine. Prospective randomized studies (table 2) reveal an incidence of TNS after lidocaine spinal anesthesia between 4 and 33%.[86] The radiating quality of the pain and initial association with spinal 5% hyperbaric lidocaine led to questions regarding potential for neurotoxicity with standard clinical doses and concentrations of lidocaine for spinal anesthesia. Contemporary reports of cauda equina syndrome after continuous lidocaine spinal anesthesia and the potential concentration-dependent neu-

rotoxicity of lidocaine have led several investigators to label TNS as manifestation of subclinical neurotoxicity.

Risk of TNS is increased with use of lidocaine (OR, 5.1 *vs.* bupivacaine), ambulatory anesthesia (OR, 1.6), lithotomy and knee arthroscopy positions (OR, 2.6) and is unaffected by baricity, dose, or dilution of lidocaine to 0.5%.[86,88] TNS typically occurs 12–36 h after resolution of spinal anesthesia, lasts for 2–3 days, and is typically rated as a 3–4/10 for pain intensity (0 = no pain, 10 = worst pain).[86,87,90,92,97,178] Discomfort from TNS is self-limited and can be effectively treated with potent nonsteroidal antiinflammatory drugs.[63,86]

Neurotoxic causes for TNS remains speculative. Patients reporting TNS do not develop sensory or motor deficits, in contrast to cauda equina syndrome. Imaging of the central nervous system does not show evidence of injury to spinal cord or nerve roots in patients with TNS. Sensitive measures of neural electrophysiology (somatosensory evoked potentials, electromyography, nerve conduction velocity, H reflex, F waves) do not change during TNS as compared with before spinal anesthesia.[177] Laboratory work in both intrathecal and desheathed peripheral-nerve models indicate that concentration of lidocaine (> 1%) is a critical factor in the neurotoxicity[63] of desheathed peripheral nerves. However, clinical trials report high incidences of TNS (17%) with spinal injection of very dilute lidocaine concentrations (0.5%, 1%)[86] that touch on the minimal effective concentration for spinal lidocaine (0.0–0.7%).[75] Indeed, further dilution of lidocaine should occur as a result of active mixing in spinal CSF[9] after nonpreferential distribution of hyperbaric solution with typical, clinical use of small-gauge pencil-point needles.[179] These clinical observations lessen the plausibility of a concentration-dependent neurotoxic cause. Finally, successful treatment of TNS with trigger point injections and nonsteroidal antiinflammatory drugs also fail to substantiate neurologic injury as a cause.[180] Other potential causes for TNS include needle trauma, patient, muscle spasm, myofascial trigger points, and early mobilization.[63] Clearly, the cause of TNS remains undetermined, and further studies are needed to elucidate the mechanism of TNS.

Postdural Puncture Headache

The first successful spinal anesthetic by August Bier was accompanied by a classic description of PDPH. Bier speculated that this headache was related to loss of CSF,[1] and this concept for mechanism of PDPH and resultant prevention has not really changed up to the present.

Although not life-threatening, PDPH carries substantial morbidity by restricting activities of daily life. A recent survey of 75 consecutive patients suffering from PDPH revealed that approximately 60% of affected patients were able to be treated with mild analgesics until spontaneous resolution of PDPH. However, approximately 18% of these patients had slight restriction of physical activity, 31% were partially bedridden with restricted physical activity, and 51% were entirely bedridden. Furthermore, spontaneous resolution of PDPH takes 1 (70% of affected patients) to 6 (95% of affected patients) weeks after dural puncture, thus resulting in frequent and prolonged restriction of daily activities.[181] Current noninvasive treatments (bed rest, fluids, analgesics, caffeine, sumatriptan) only temporize the discomfort.[182] Epidural blood patch remains the invasive treatment of choice, with approximately 70% prolonged success after initial injection.[183,184] Epidural patching with nonblood substances (*e.g.*, saline or colloid) are ineffective for prolonged relief,[184] although other substances such as fibrin glue are being examined.[185]

Traditional concepts suggest that dural puncture causes a leak of CSF with resultant loss of CSF pressure, gravitational traction of brain structures, and painful neurovascular response from the meninges. Recent data support this empiric mechanism of CSF loss causing PDPH, as MRI correlates CSF loss with PDPH.[186] There is also MRI imaging evidence for meningeal involvement in pain generation, as meningeal structures are enhanced by gadolinium during but not after PDPH, suggesting localized changes in the blood–brain barrier during PDPH.[187] Injection of 20 ml blood into the epidural space of patients suffering from PDPH creates an immediate tamponade effect on spinal CSF extending approximately five vertebral segments on MRI imaging. These findings are consistent with both the immediate (tamponade) and prolonged (cessation of CSF leak) relief from epidural blood patch.[183]

Because no effective noninvasive treatments exist, clinical strategies have focused on prophylactically reducing CSF loss after dural puncture. Traditionally, we have minimized needle size to decrease the size of the CSF leak in the dura, turned cutting bevels longitudinally to prevent transverse cutting of longitudinally aligned dural fibers, and selected pencil-point needles to maximize the parting and not cutting of dural fibers. Although these clinical strategies are effective in decreasing incidence of PDPH,[71] evidence for these mechanisms has been conflicting. Smaller needle size, pencil point, and longitudinal bevel direction have been shown *in vitro* to result in less CSF leakage.[188] However, electron microscopic evaluation of the dura suggests that fibers do not run longitudinally but in a more random organization, questioning the concept that longitudinal dural fibers are parted by longitudinal bevels and pencil-point needles.[186] An alternative explanation for decreased loss of CSF with longitudinally oriented needle bevels is that the dura is under longitudinal tension, and a longitudinal puncture will tend to be pulled close. Reina *et al.*[186] also question the concept of less trauma to the dura with pencil-point needles, as their study observed similarly sized, more traumatic lesions to the dura with pencil-point needles compared with longitudinally aligned cutting tips. The investigators propose an intriguing hypoth-

Table 5. Pharmacologic Activities of Anticoagulant Agents

Agent	Effect on Coagulation Tests		Peak Effect	Return of Hemostasis after Discontinuation	Comments and Recommendations
	PT	APTT			
Intravenous heparin	+	+++	Minutes	4–6 h	Monitor ACT, APTT, start heparin ≥ 1 h after spinal, stop heparin 3–4 h before spinal and check APTT
Subcutaneous heparin	+	++	1–2 h	4–6 h	APTT usually normal; avoid spinal during peak effect
LMWH	—	—	3–5 h	12+ h	Anti-Xa reflects anticoagulation; start LMWH 24 h after spinal; stop LMWH 12–24 h before spinal
Warfarin type	+++	+	2–6 days	4–6 days	Monitor PT; avoid spinal until PT normal
Antiplatelet					
Aspirin	—	—	h	5–8 days	By themselves, no evidence for increased risk
Other NSAIDs	—	—	h	1–3 days	

PT = prothombin time; APTT = activated partial thromboplastin time; ACT = activated clotting time; + = clinically insignificant increase; ++ = possibly clinically significant increase; +++ = clinically significant increase; LMWH = low-molecular-weight heparin; NSAIDs = nonsteroidal antiinflammatory drugs.

Data are from references 176 and 196.

esis that the more traumatic lesion from the pencil-point needle forms an inflammatory plug to reduce CSF loss and minimize PDPH. Although mechanisms are not fully elucidated, there is excellent support for use of small-gauge pencil-point needles to reduce the incidence of PDPH. Other reasons to use pencil-point needles include fewer manufacturing flaws, less susceptibility to tip damage after bony contact, and less likelihood of deposition of tissue cores into the CSF than cutting needles.[189,190]

Anticoagulants

Anticoagulants are frequently used in the surgical population as prophylaxis and treatment for thrombotic conditions. Analysis of closed claims for neurologic injury indicates that anticoagulation is a major risk factor for spinal cord injury with spinal anesthesia.[191] Estimated incidence of spinal hematoma with spinal anesthesia in the absence of anticoagulation is estimated at 1:220,000.[176] Clearly, with such a small baseline incidence, it is very difficult to assess increased risk from different classes of anticoagulants without data from hundreds of thousands to millions of patients. As no such data exist, much of our practice is based on small surveys, anecdotal reports, and expert opinion (table 5).[176,192]

Antiplatelet Agents. Several small studies have documented the relative safety of performing spinal anesthesia in patients receiving irreversible (aspirin) and temporary (other nonsteroidal antiinflammatory drugs, ibuprofen) antiplatelet agents.[176] A prospective survey of 1,000 patients receiving antiplatelet agents did not note an increased incidence of hemorraghic needle placement.[193] Expert opinion considers risk of antiplatelet agents to be minimal,[176] but there are case reports of spinal hematoma associated with spinal anesthesia and antiplatelet agents.[194] Caution and judgment should be exercised when patients are receiving other anticoagulants in addition to antiplatelet agents because of augmented anticoagulation effects.[176]

Oral Anticoagulants. Several small studies have documented the relative safety of performing spinal anesthesia in patients with mild anticoagulation from oral warfarin-type anticoagulants.[176] Prospective and retrospective surveys of 459–1,000 patients receiving oral anticoagulants did not document any neurologic complications with epidural and spinal anesthesia.[176] Anticoagulant activity in most of these surveys was mild as evidenced by international normalized ratios of 1.4 or less, and spinal hematomas have been reported with oral anticoagulants and central neuraxial block.[195] Expert opinion on management of these patients suggests withholding oral agents and normalizing coagulation where possible.[192]

Standard Heparin. Subcutaneous heparin appears to add little risk to spinal anesthesia.[196] A review of more than 5,000 patients noted no spinal hematomas in patients receiving subcutaneous heparin and central neuraxial blocks.[176] However, systemic anticoagulation may occur, and spinal hematoma has been described with subcutaneous heparin and epidural block.[176,197] Risk of neurologic complications may be reduced by giving the heparin after spinal puncture and may be increased in debilitated patients or after long duration of therapy.[176]

Epidural and spinal blocks before intraoperative therapeutic anticoagulation with heparin has been studied in series of 342–4,000 patients.[196] Previous investigators observed minimal complications when needle placement was atraumatic, heparin was initiated at least 60 min after block, and no other anticoagulants were used.[176,196] Spinal puncture should be avoided if the patient is currently systemically anticoagulated with heparin. The heparin should then be stopped for 2–4 h, and an activated partial thromboplastin time checked to verify normal coagulation before spinal puncture.[192]

Low-molecular-weight Heparin. Low-molecular-weight heparin (LMWH) is a fractionated component of

standard heparin (4,000–6,500 d *vs.* 12,000–15,000 for standard heparin). LMWH has much greater bioavailability, primarily affects coagulation factor X, and can not be monitored with activated partial thromboplastin time.[198] More than a decade of European experience suggested that perioperative use of LMWH did not add substantial risk to spinal anesthesia.[199] However, the US experience has been far different, with more than 40 cases of spinal hematomas since its introduction in 1993. In contrast to European experience of relative safety, estimates of risk of spinal hematoma with LMWH and spinal anesthesia in the United States is 1:41,000 *versus* the 1:225,000 in the non-anticoagulated patient.[176] Larger daily dose and more frequent administration with US practice may account for this apparent increase in risk. Guidelines to safe use of LMWH and spinal anesthesia include delay of administration of LMWH for at least 24 h after spinal puncture. If the patient is already using LMWH, then it should be stopped for at least 12–24 h for higher doses (*e.g.*, 1 mg/kg enoxaparin twice daily) before spinal puncture.[176,192]

Conclusion

Spinal anesthesia is an old, simple, and popular anesthetic technique, yet much remains unknown regarding pertinent anatomy, physiology, and pharmacology. This article reviewed how classical concepts on anatomy and mechanisms of action of spinal anesthesia are being questioned and expanded in scope. Investigations into physiologic effects of spinal anesthesia reveal complex actions on multiple organ systems. New local anesthetics, analgesic additives, and techniques are being investigated for different applications as the practice of medicine focuses on outpatient care. Safety of spinal agents and complications from spinal anesthesia continue to be examined and reexamined to improve safety. Further study will be needed to fully resolve the issues discussed in this article and to further understand and improve the clinical use of spinal anesthesia.

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