19 Regional Anesthesia and Infection

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Infectious complications may occur after any regional anesthetic techniques, but are of greatest concern if the infection occurs around the spinal cord or within the spinal canal. Possible risk factors include underlying sepsis, diabetes, depressed immune status, steroid therapy, localized bacterial colonization or infection, and chronic catheter maintenance. Bacterial infection of the central neural axis may present as meningitis or cord compression secondary to abscess formation. The infectious source for meningitis and epidural abscess may result from distant colonization or localized infection with subsequent hematogenous spread and central nervous system (CNS) invasion. The anesthetist may also transmit microorganisms *directly* into the CNS by needle/catheter contamination through a break in aseptic technique or passage through a contiguous infection. An indwelling neuraxial catheter, although aseptically sited, may be colonized with skin flora and consequently serve as a source for ascending infection to the epidural or intrathecal space.

Historically, the frequency of serious CNS infections such as arachnoiditis, meningitis, and abscess after spinal or epidural anesthesia was considered to be extremely low – cases were reported as individual cases or small series.[1-3] However, recent epidemiologic series from Europe suggest that the frequency of infectious complications associated with neuraxial techniques may be increasing.[4,5] In a national study conducted from 1997 to 1998 in Denmark, Wang et al.[5] calculated the risk of *persisting* neurologic deficits to be 1:4343 following epidural analgesia. Moen et al.[4] reviewed the Swedish experience from 1990–1999 and reported a low incidence of epidural abscess, but an alarming association of post–spinal block meningitis with α-hemolytic streptococcal cultures, suggesting a nosocomial origin.

This chapter will discuss the clinical presentation of CNS infections, the laboratory and clinical studies evaluating the association between meningitis and dural puncture in bacteremic subjects, and the risk of infection during short-term and chronic epidural catheterization in febrile and immunocompromised patients, including those with herpes simplex virus (HSV) and human immunodeficiency virus (HIV). Finally, the importance and implications of aseptic techniques will be presented.

Epidemiology of Meningitis and Epidural Abscess

Bacterial meningitis is the most common form of CNS infection, with an annual incidence in the United States of >2.5 cases/100,000 population. The epidemiology of bacterial meningitis has changed significantly in recent years, following the

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introduction and increasingly widespread use of vaccines for *Haemophilus influenzae* and *Neisseria meningitidis*. Currently, *Streptococcus pneumoniae* accounts for nearly two-thirds of community acquired meningitis; causative organisms of nosocomial meningitis include gram-negative bacilli, *Staphylococcus aureus* and coagulase-negative staphylococci.

Most cases of meningitis are associated with a recent infection (particularly otic or respiratory) or head trauma. Meningitis after spinal anesthesia has been only rarely reported. In a study evaluating the frequency of meningitis in patients undergoing spinal anesthesia, Kilpatrick and Girgis[6] retrospectively reviewed the records of all patients admitted to the meningitis ward in Cairo, Egypt. During a 5-year period from 1975 to 1980, 17 of 1429 patients admitted with a diagnosis of meningitis had a history of recent spinal anesthesia. The patients developed meningeal symptoms 2–30 days (mean 9 days) after spinal anesthesia and were symptomatic for 1–83 days (mean 15 days) before hospital admission. Ten of the 17 had positive cerebrospinal fluid (CSF) cultures; eight were *Pseudomonas aeruginosa*, one was *S. aureus*, and one was *S. mitis*. These organisms were not cultured from patients who had not had spinal anesthesia. Two additional patients with a history of recent spinal anesthesia demonstrated evidence of tuberculous meningitis. The lack of positive CSF cultures was presumed to be a result of oral antibiotic therapy which was present in more than half of patients at the time of admission. However, all patients, including those with negative CSF cultures, were treated with antibiotic therapy. Four of the 17 patients died. These results suggest that meningitis in patients with a history of recent spinal anesthesia is often the result of unusual or nosocomial organisms and that aggressive bacteriologic evaluation and antibiotic coverage are warranted.

Most epidural abscesses are not related to the placement of indwelling catheters, but are believed to be related to infections of the skin, soft tissue, spine, or hematogenous spread to the epidural space.[7] In a large retrospective review, epidural abscess accounted for 2–12 cases per 100,000 admissions to tertiary hospitals.[2] The most frequently identified organisms were *S. aureus* (57%), streptococci (18%), and gram-negative bacilli (13%). The source of infection was most often attributed to osteomyelitis (38%), bacteremia (26%), and postoperative infection (16%). Only one of the 39 cases was related to an epidural catheter. In a more recent review, Ericsson et al.[3] reported 10 cases of epidural abscess. Four of these were associated with invasive spinal procedures including repeated lumbar punctures in the presence of meningitis (two cases), epidural catheter (one case), and a paravertebral anesthetic injection (one case). In a retrospective study, Danner and Hartman[8] reported no spinal infections related to epidural anesthesia/analgesia. These authors were able to characterize the clinical course of epidural abscess, as well as identify risk factors for neurologic recovery. Diagnosis was more difficult and often delayed in patients with chronic epidural abscesses, because these patients were less likely to be febrile or have an increased leukocyte count compared with patients with acute abscesses. However, rapid neurologic deterioration could occur in either group. In addition, earlier diagnosis and treatment improved neurologic outcome. Steroid administration and increased neurologic impairment at the time of surgery adversely affected outcome.

Meningitis and Epidural Abscess after Neuraxial Anesthesia

Neuraxial anesthesia is a rare etiology of CNS infections[4,5,9–18] (Table 19-1). For example, in a combined series of more than 65,000 spinal anesthetics, there were only three cases of meningitis. A similar review of approximately 50,000 epidural anesthetics failed to disclose a single epidural or intrathecal infection.[18] Aromaa et al.[17] reported eight cases of bacterial infections in patients undergoing 170,000 epidural and 550,000 spinal anesthetics (1.1:100,000 blocks) from a Finnish database. More

TABLE 19-1. Infectious Complications following regional Anesthesia

Author, year	No. of patients	Population	Neuraxial techniques	Antibiotic prophylaxis	Duration of indwelling catheter	Complications
Kane,[18] 1981	115,000	Surgical and obstetric	65,000 spinal 50,000 epidural	Unknown	Unknown	3 meningitis (all after spinal anesthesia)
Du Pen et al.,[9] 1990	350	Cancer and AIDS patients	Permanent (tunneled) epidural analgesia	No	4–1,460 days	30 insertion site infections, 19 deep track or epidural space infections; treated with catheter removal and antibiotics, 15 uneventfully replaced
Scott and Hibbard,[10] 1990	505,000	Obstetric	Epidural	Unknown	Unknown	1 epidural abscess; laminectomy with partial recovery
Bader et al.,[11] 1992	319	Parturients with chorioamnionitis	General (26), epidural (224), spinal (29), local (50) anesthesia	Yes (13%)	Surgical	None
Strafford et al.,[12] 1995	1,620	Pediatric surgical	Epidural analgesia	No	2.4 days median	3 positive epidural catheter tip cultures 1 *Candida* colonization of epidural space (along with necrotic tumor)
Goodman et al.,[13] 1996	531	Parturients with chorioamnionitis	Spinal (14), epidural (517) anesthesia and analgesia	Yes (23%)	24 hours (64 patients)	None
Dahlgren and Tornebrandt,[14] 1995	18,000	All indications and ages of patients	Spinal (8768) and epidural (9232)	Unknown	Unknown	None
Kindler et al.,[15] 1996	13,000	4,000 obstetric 9,000 surgical	Epidural	Unknown	Unknown	2 epidural abscess, both requiring laminectomy
Auroy et al.,[16] 1997	71,053	Surgical	Spinal (40,640) Epidural (30,413)	Unknown	Unknown	None
Aromaa et al.,[17] 1997	720,000	Surgical	Epidural (170,000) Spinal (550,000)	Unknown	Unknown	4 meningitis 2 epidural abscess 2 discitis 2 superficial skin infections
Wang et al.,[5] 1999	17,372	Surgical, cancer, and trauma	Epidural	Unknown	11 days mean 6 days median	9 epidural abscess; 7 required laminectomy; complete recovery in 6 of 10 patients 2 subcutaneous infections
Moen et al.,[4] 2004	1,710,000	Pain, surgical, and obstetric	Spinal (1,260,000) Epidural (450,000)	Unknown	2 days–5 weeks	29 meningitis; partial sequelae in 6 patients 13 epidural abscess, laminectomy performed in six patients; 4 of 5 patients with deficits did not recover

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recent epidemiologic series are alarming. In a national study conducted from 1997 to 1998 in Denmark, Wang et al.[5] reported the incidence of epidural abscess after epidural analgesia was 1:1930 catheters. Patients with epidural abscess had an extended duration of epidural catheterization (median 6 days, range 3–31 days). In addition, the majority of the patients with epidural abscess were immunocompromised. Often the diagnosis was delayed; the time from first symptom to confirmation of the diagnosis was a median of 5 days. *S. aureus* was isolated in 67% of patients. Patients without neurologic deficits were successfully treated with antibiotics, whereas those with deficits underwent surgical decompression (typically with only moderate neurologic recovery). It is difficult to determine why the frequency of symptomatic epidural abscess was so high in this series. Because perioperative antithrombotic therapy was involved in most cases, it is possible that the epidural abscesses were infected epidural hematomas, but this is not strongly supported by the diagnostic imaging studies and neurosurgical findings.

In a retrospective series from Sweden involving 1,260,000 spinal and 450,000 epidural anesthetics (including 200,000 placed for labor analgesia) performed over a decade, Moen et al.[4] reported 42 serious infectious complications. Epidural abscess occurred in 13 patients; nine (70%) were considered immunocompromised as a result of diabetes, steroid therapy, cancer, or alcoholism. Six patients underwent epidural block for analgesia after trauma. The time from placement of the epidural catheter to first symptoms ranged from 2 days to 5 weeks (median 5 days). Although prevailing symptoms were fever and severe backache, five developed neurologic deficits. All seven positive cultures isolated *S. aureus*. Overall neurologic recovery was complete in seven of 12 patients. However, four of the five patients with neurologic symptoms did not recover.

Meningitis was reported in 29 patients for an overall incidence of 1:53,000. A documented perforation of the dura (intentional or accidental) occurred in 25 of 29 cases. Unlike the cases of epidural abscess, which tended to be reported in immunocompromised patients, the patients who developed meningitis following spinal anesthesia were reportedly healthy and undergoing minor surgical procedures. The time interval between neuraxial block and symptoms varied from 8 hours to 8 days (median 24 hours). Importantly, all patients complained of headache, but the classic symptoms of meningitis (fever, headache, and nuchal rigidity) were present in only 14 patients. In the 12 patients in whom positive cultures were obtained, alpha-hemolytic streptococci were isolated in 11 patients and *S. aureus* in one. Meningitis resulted in residual neurologic deficits in six patients.

These large epidemiologic studies represent new and unexpected findings regarding the demographics, frequency, etiology, and prognosis of infectious complications following neuraxial anesthesia. Epidural abscess is most likely to occur in immunocompromised patients with prolonged durations of epidural catheterization. The most common causative organism is *S. aureus*, which suggests the colonization and subsequent infection from normal skin flora as the pathogenesis. Delays in diagnosis and treatment result in poor neurologic recovery, despite surgical decompression. Conversely, patients who develop meningitis following neuraxial blockade typically are healthy and have undergone uneventful spinal anesthesia. Furthermore, the series by Moen et al. validates the findings of individual case reports of meningitis after spinal anesthesia – the source of the pathogen is mostly likely to be the upper airway of the proceduralist.[19–22] Although the frequency of serious infectious complications is much higher than reported previously, the results may be attributable to differences in reporting and/or clinical practice (asepsis, perioperative antibiotic therapy, duration of epidural catheterization).[4,5] Finally, although recent investigations have substantially illuminated the etiology, risk factors, and prognosis of infectious complications after neuraxial blockade, similar information for patients undergoing peripheral regional anesthetic techniques and invasive pain procedures is limited.[23–26]

Neuraxial Blockade in the Febrile (Bacteremic) or Infected Patient

Few data suggest that spinal or epidural anesthesia during bacteremia is a risk factor for infection of the central neural axis. Although the authors of previous studies[4,5,14,18] did not report how many patients were febrile during administration of the spinal or epidural anesthetic, a significant number of the patients included in these studies underwent obstetric or urologic procedures, and it is likely that some patients had bacteremia after (and perhaps during) needle or catheter placement. Despite the apparent low risk of CNS infection following regional anesthesia, anesthesiologists have long considered sepsis to be a relative contraindication to the administration of spinal or epidural anesthesia. This impression is based largely on anecdotal reports and conflicting laboratory and clinical investigations.

Meningitis after Dural Puncture

Dural puncture has long been considered a risk factor in the pathogenesis of meningitis. Exactly how bacteria cross from the blood stream into the spinal fluid is unknown. The presumed mechanisms include introduction of blood into the intrathecal space during needle placement and disruption of the protection provided by the blood-brain barrier. However, lumbar puncture is often performed in patients with fever or infection of unknown origin. If dural puncture during bacteremia results in meningitis, definite clinical data should exist. In fact, clinical studies are few, and often antiquated.

Initial clinical[27–31] and laboratory[32] investigations were performed more than 80 years ago (Table 19-2). In 1919, Weed et al.[32] demonstrated that lumbar or cisternal

TABLE 19-2. Meningitis after Dural Puncture

Author, year	No. of patients	Population	Microorganism (s)	Patients with spontaneous meningitis	Patients with lumbar puncture–induced meningitis	Comments
Wegeforth and Latham,[27] 1919	93	Military personnel	*N. meningitidis* *S. pneumonia*	38 of 93 (41%)	5 of 93, including 5 of 6 bacteremic patients	Lumbar punctures performed during meningitis epidemics
Pray,[28] 1941	416	Pediatric with bacteremia	*S. pneumonia*	86 of 386 (22%)	8 of 30 (27%)	80% of patients with meningitis <2 years of age
Eng and Seligman,[29] 1981	1,089	Adults with bacteremia	Atypical and typical bacteria	30 of 919 (3.3%)	3 of 170 (1.8%)	Atypical organisms responsible for lumbar puncture–induced meningitis
Teele et al.,[30] 1981	271	Pediatric with bacteremia	*S. pneumonia* *N. meningitidiss* *H. influenza*	2 of 31 (9%)	7 of 46 (15%)*	All cases of meningitis occurred in children <1 year of age. Antibiotic therapy reduced risk
Smith et al.,[31] 1986	11	Preterm with neonatal sepsis		0%	0%	

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*Significant association ($P < .001$).

Spontaneous meningitis = concurrent bacteremia and meningitis (without a preceding lumbar puncture); lumbar puncture–induced meningitis = positive blood culture with sterile CSF on initial examination; subsequent positive CSF culture (same organism present in blood).

puncture performed during septicemia (produced by lethal doses of an intravenously administered gram-negative bacillus) invariably resulted in a fatal meningitis. In the same year, Wegeforth and Latham[27] reported their clinical observations of 93 patients suspected of having meningitis who received a diagnostic lumbar puncture. Blood cultures were taken simultaneously. The diagnosis was confirmed in 38 patients. The remaining 55 patients had normal CSF. However, six of these 55 patients were bacteremic at the time of lumbar puncture. Five of the six bacteremic patients subsequently developed meningitis. It was implied, but not stated, that patients with both sterile blood and CSF cultures did not develop meningitis. Unfortunately, these lumbar punctures were performed during two epidemics of meningitis occurring at a military instillation, and it is possible that some (or all) of these patients may have developed meningitis without lumbar puncture. These two historical studies provided support for the claim that lumbar puncture during bacteremia was a possible risk factor for meningitis.

Subsequent clinical studies reported conflicting results. Pray[28] studied the incidence of pneumococcal meningitis in children who underwent a diagnostic lumbar puncture during pneumococcal sepsis. The incidence of meningitis was no greater among patients who were subjected to lumbar puncture, which produced normal CSF (8 of 30 patients, or 27%), than among those who did not undergo diagnostic spinal tap (86 of 386 patients, or 22%). Eng and Seligman[29] retrospectively reviewed the records of 1089 bacteremic patients, including 200 patients who underwent lumbar puncture. The authors reported that the incidence of meningitis after lumbar puncture did not significantly differ from the incidence of spontaneous meningitis and concluded: "If lumbar puncture induced meningitis does occur, it is rare enough to be clinically insignificant."

However, not all studies have been as reassuring as those described above. In a review of meningitis associated with serial lumbar punctures to treat posthemorrhagic hydrocephalus in premature infants, Smith et al.[31] attempted to identify risk factors. Six of 22 (27%) infants undergoing multiple (2–33) therapeutic dural punctures during a period of 2–63 days developed meningitis. Bacteremia, a risk factor for meningitis in this report, was associated with central venous or umbilical artery catheters. However, 11 septic infants who underwent dural puncture did not develop meningitis. The number of dural punctures, incidence of "difficult or traumatic" procedures, and use of antibiotics did not differ between infants who developed meningitis and those who did not. A causal relationship between the dural puncture and onset of meningitis was not clear. Teele et al.[30] retrospectively reviewed the records of 277 bacteremic children during a 10-year interval from 1971–1980. Meningitis occurred in 7 of 46 (15%) children with normal CSF obtained during a bacteremia. However, only 2 of 231 (1%) children who did not undergo lumbar puncture developed meningitis. These results were significantly different. In addition, children treated with antibiotics at the time of lumbar puncture were less likely to develop meningitis than children who were not treated until after lumbar puncture. The authors admitted that clinical judgment may have allowed the pediatricians to select the child in whom meningitis is developing before the CSF is diagnostic; these patients may appear more ill and thus suggest the performance of a lumbar puncture.

Prevention of lumbar puncture–induced meningitis with antibiotic therapy is supported by a more recent animal study. Carp and Bailey[33] investigated the association between meningitis and dural puncture in bacteremic rats. Twelve of 40 rats subjected to cisternal puncture with a 26-gauge needle during an *Escherichia coli* bacteremia subsequently developed meningitis. Meningitis occurred only in animals with a blood culture result of $\geq$50 colony forming units/mL at the time of dural puncture, a circulating bacterial count observed in patients with infective endocarditis. In addition, bacteremic animals not undergoing dural puncture, as well as animals undergoing dural puncture in the absence of bacteremia, did not develop meningitis. Treatment of a group of bacteremic rats with a single dose of gentamicin immediately before

cisternal puncture eliminated the risk of meningitis; none of these animals developed infection.

This study demonstrates that dural puncture in the presence of bacteremia is associated with the development of meningitis in rats, and that antibiotic treatment before dural puncture reduces this risk. Unfortunately, this study did not include a group of animals that were treated with antibiotics *after* dural puncture. Because many surgeons defer antibiotic therapy until after cultures are obtained, the actual clinical scenario remains unstudied. There are several other limitations to this study. Whereas *E. coli* is a common cause of bacteremia, it is an uncommon cause of meningitis. In addition, the authors knew the sensitivity to the bacteria injected, allowing for appropriate antibiotic coverage. The authors also performed a cisternal puncture (rather than lumbar puncture) and used a 26-gauge needle, producing a relatively large dural defect in the rat compared with humans, and no local anesthetic was injected. Local anesthetic solutions are bacteriostatic, which may theoretically reduce the risk of meningitis in normal clinical settings. Whereas these results may apply to the performance of spinal anesthesia in the bacteremic patient, they do not apply to administration of epidural anesthesia in the febrile patient, which is associated with a higher incidence of vascular injury and typically involves placement of an indwelling foreign body.

Meningitis after Spinal and Epidural Anesthesia

Even when meningitis occurs temporally after spinal anesthesia, it is often difficult to establish a cause-and-effect relationship between spinal anesthesia and meningitis. The following case report describes a probable case of lumbar puncture–induced meningitis.[34] A 60-year-old man underwent kidney stone removal under general anesthesia. On postoperative day six, the patient remained afebrile, but was taken to the operating suite for transurethral clot evacuation. Spinal anesthesia was performed under aseptic technique. CSF was clear. Forty minutes later, shaking chills developed. Initial blood and urine cultures were negative. The following day, the patient became febrile and complained of headache and back pain and appeared confused. CSF examination revealed cloudy CSF with a leukocytosis (80% polymorphonucleocytes), decreased glucose concentration consistent with bacterial infection, but no growth on culture. Three days later, a repeat lumbar puncture was performed with similar results. A third lumbar puncture was performed 2 days later; culture yielded group D streptococcus (enterococci). Group D enterococci are unusual sources of meningitis. In this case it is possible, although unlikely, that the patient was bacteremic before administration of the spinal anesthetic. It is more likely that the bacteria entered the blood stream during bladder irrigation (because bacteremia occurs in perhaps 60% of urologic procedures) and traversed the dura at the puncture site, similar to the animals in the study by Carp and Bailey.[33] However, despite the apparent temporal association, it is difficult to prove that the presence of a prebacteremic dural puncture increased the risk of subsequent meningitis in this patient.

Bacterial meningitis can also present after epidural blockade with or without a localized epidural abscess.[1,35] In a rare report, Ready and Helfer[1] described two cases of meningitis following the use of epidural catheters in parturients. In the first case, a healthy 28-year-old parturient underwent lumbar epidural catheter placement for elective cesarean delivery. The epidural analgesia was provided for 48 hours postoperatively with an opioid. At the time of removal, a 4-cm erythematous indurated area, which was tender to palpation, was noted at the catheter entry site. Three days later, the patient complained of severe headache, nuchal rigidity, and photophobia. An area of cellulitis was present at the epidural insertion site. CSF examinations revealed an increased protein (308 mg/dL), decreased glucose (27 mg/dL), and 3000 leukocytes/μL (73% polymorphonucleocytes). Culture of the CSF was positive for *S. faecalis*. Urine and blood cultures were negative. There was no evidence of epidural abscess

on magnetic resonance imaging scan. Antibiotic therapy was initiated and the patient completely recovered. Although it was thought the most likely source of the meningitis was the area of cellulitis surrounding the epidural catheter insertion site, the possibility of alternative causes could not be excluded.

In the second case, a lumbar epidural was placed in a healthy 25-year-old parturient. Delivery occurred uneventfully 50 minutes later, and the catheter was removed. No local inflammation was noted at the catheter insertion site. The patient reported a nonpositional headache and neck stiffness 24 hours later. Lumbar puncture revealed increased protein (356 mg/dL), decreased glucose (5 mg/dL), and 4721 leukocytes/μL (90% polymorphonucleocytes). CSF cultured positive for *S. uberis* (a strain of α-hemolytic streptococcus). However, urine, blood, and vaginal cultures also grew the same organism. Antibiotic therapy was initiated, and recovery was complete. The short duration of the indwelling catheter, the lack of physical findings suggestive of infection at the catheter insertion site, and the presence of the organism in vaginal secretions, blood, and urine suggest that the source of the meningitis was most likely hematogenous spread of the infecting organism from the vagina.[1] The case reported by Berman and Eisele,[34] and the two cases by Ready and Helfer[1] demonstrate how a cause-and-effect relationship should not be assumed between the regional anesthetic and the CNS infection, but rather other possible sources should be investigated.

Epidural Abscess after Epidural Anesthesia

Several relevant studies have specifically examined the risk of epidural abscess in bacteremic patients receiving epidural anesthesia and/or analgesia. The anesthesiologist is frequently faced with the management of the parturient with suspected chorioamnionitis, approximately 8% of whom are bacteremic. Bader et al.[11] investigated the use of regional anesthesia in women with chorioamnionitis. Three hundred nineteen women were identified from a total of 10,047 deliveries. Of the 319 women, 100 had blood cultures taken on the day of delivery. Eight of these had blood cultures consistent with bacteremia. Two hundred ninety-three of the 319 patients received a regional anesthetic; in 43 patients, antibiotics were administered before needle or catheter placement. No patients in the study, including those with documented bacteremias, had infectious complications. In addition, mean temperatures and leukocyte counts in patients who received blood cultures showed no significant differences between bacteremic and nonbacteremic groups. Goodman et al.[13] also retrospectively reviewed the hospital records of 531 parturients who received epidural or spinal anesthesia and were subsequently diagnosed with chorioamnionitis. Blood cultures were drawn in 146 patients; 13 were positive. Antibiotics were administered before the regional block was placed in only 123 patients, whereas nearly one-third of patients did not receive antibiotic therapy in the entire peripartum period. As with the study by Bader et al.,[11] leukocytosis, fever, abdominal tenderness, or foul-smelling discharge were not predictors of positive blood cultures. There were no infectious complications. These authors continue to administer spinal and epidural anesthesia in patients with suspected chorioamnionitis because the potential benefits of regional anesthesia outweigh the theoretical risk of infectious complications. However, the small number of patients with documented bacteremias in both studies defies a definitive statement regarding the risk of CNS infections in patients suspected of chorioamnionitis undergoing regional anesthetic techniques.

Few data exist regarding the placement and maintenance of epidural catheters in patients with an infection at a site distant from the neuraxis. Darchy et al.[36] studied 75 patients in the intensive care unit receiving epidural analgesia (median 4 days), including 21 patients with a known localized concomitant infection. Although five patients had catheter insertion site inflammation/erythema (with or without positive epidural catheter culture), the frequency was not increased by the presence of an

infectious source distant to the epidural catheter site. However, the authors recommended a meticulous daily inspection of the catheter insertion site and immediate removal of the catheter if both erythema and local discharge are present, because these two signs of local inflammation are predictors of positive epidural catheter colonization/infection.

Factors Affecting Bacterial Colonization During Epidural Catheterization

Although the epidural catheter tip is frequently colonized, progression to epidural space infection rarely occurs.[9,36] The low frequency of significant epidural infection (1–2 cases per 10,000 hospital admissions)[2] associated with epidural catheter placement is especially notable when compared with the frequency of intravenous catheter-related septicemia, which approaches 1%, or greater than 50,000 cases annually. Several factors may contribute to the low incidence of epidural space infections, including meticulous attention to aseptic technique, careful monitoring of catheter insertion site, antibiotic prophylaxis, and use of bacterial filters. However, because these interventions are frequently initiated in patients with indwelling central venous catheters, additional factors unique to epidural anesthesia and analgesia, such as the bactericidal effect of local anesthetic solutions, may also contribute significantly.

Bupivacaine and lidocaine have been shown to inhibit the growth of a variety of microorganisms in culture.[37] Unfortunately, the bactericidal effect decreases significantly with concentrations of local anesthetic typically used to provide analgesia, whereas opioid solutions do not exhibit *any* ability to inhibit bacterial growth. In addition, growth of *S. aureus* and coagulase-negative staphylococci, the most frequently identified pathogens in epidural infections, is inhibited only at higher concentrations of local anesthetic, such as solutions of 2% lidocaine and 0.5% bupivacaine. Therefore, although it seems that local anesthetic solutions are unlikely to prevent epidural infections in most patients receiving epidural analgesia, it is possible that in immunocompromised patients, local anesthetics may inhibit the growth of more fastidious organisms, even at low concentrations. Further clinical studies are needed to investigate the in vivo bactericidal effects of dilute local anesthetic solutions.

The catheter hub, catheter insertion site, and hematogenous spread are three major routes of entry for microorganisms into the epidural space, with the catheter hub accounting for nearly half of the sources.[9,38,39] A bacterial filter placed at the catheter hub acts as a physical barrier for bacteria present in the infusing solution, and should theoretically reduce the incidence of epidural colonization. However, studies of epidural catheter tip cultures have reported mixed results, and cases of epidural infection after hub colonization despite the use of filters have been reported.[9,39,40] Possible explanations for hub-related epidural infections in patients with bacterial filters include a reduced antimicrobial effectiveness with prolonged use, and direct contamination of the hub during filter-changing techniques. De Cicco et al.[41] reported a positive trend between the number of filter changes and the rate of positive hub cultures. These data suggest that continued attention to aseptic technique is warranted throughout the period of epidural catheterization, and that the use of bacteriologic filters is alone unlikely to be efficacious in preventing epidural colonization and infection.[42]

Controversy exists regarding the conditions under which a disconnected epidural catheter can be safely reconnected. In an in vitro investigation, Langevin et al.[43] inoculated epidural catheters containing a 5 μ/mL fentanyl solution with *S. aureus*, *E. coli*, or *P. aeruginosa*. Eight hours after catheter contamination, providing the fluid in the catheter remained static, no bacteria were detected more than 20 cm from the contaminated catheter hub. Vertical or horizontal positioning of the catheter during incubation did not affect bacterial advancement along the catheter, as long as the fluid was displaced distally less than 20 cm. However, if the fentanyl solution was allowed to drain and advance 33 cm, bacteria were found at the epidural end of the catheter, 88 cm distally. The advancement of bacteria by fluid displacement is clinically

significant; in more than two-thirds of patients, fluid will drain by gravity into the epidural space in less than 1 hour after discontinuation of an epidural infusion. The authors concluded that the interior of a disconnected epidural catheter will remain sterile for at least 8 hours if the fluid in the catheter remains static, and the catheter may be aseptically reconnected after removal of the contaminated section. In addition, the presence of a meniscus more than 20–25 cm from the free end of a disconnected catheter may indicate contamination of the catheter tip in the epidural space, and immediate catheter removal was recommended. Unfortunately, the authors did not evaluate the advancement of bacteria in epidural catheters filled with local anesthetic solutions, or investigate the effect of a local anesthetic injected after the bacterial inoculation and incubation.

Neuraxial Blockade in the Immunocompromised Patient

Large series have demonstrated that patients with altered immune status are at increased risk for infectious complications (Table 19-3).[4,5] Strafford et al.[12] reviewed 1620 pediatric patients who received epidural analgesia for postoperative pain relief. Epidural catheters were left indwelling for a median of 2 days (range, 0–8 days). No patient developed an epidural abscess. One patient with osteosarcoma metastatic spread to spine, chest wall, and lungs became febrile after 10 days of epidural catheterization. The catheter was removed, and a culture demonstrated candidal contamination. A second thoracic epidural catheter was placed 4 days later to provide superior analgesia. Two weeks later, she developed an acute sensory and motor block at T2. Magnetic resonance imaging showed an epidural fluid collection; an emergent laminectomy was performed. A large amount of necrotic tumor as well as fluid containing *Candida tropicalis* was present in the epidural space. Her neurologic deficits resolved postoperatively. Three additional patients with chronic pain syndromes were evaluated for epidural infection, but all were negative. The authors concluded that for terminally ill patients, the risk of infection with long-term epidural catheterization is acceptable, but recommended careful monitoring to avoid serious neurologic sequelae.

Chronic epidural catheterization in immunocompromised patients is also a potential risk for epidural infection. Du Pen et al.[9] studied 350 cancer and HIV-infected patients in whom permanent (tunneled) epidural catheters were placed. The authors examined three areas of the catheter track for evidence of infection: exit site, superficial catheter track, and epidural space. The rate of epidural and deep track catheter-related infections was one in every 1702 days of catheter use in the 19 patients who developed deep track (8) or epidural (15) infections. (Four of the 19 patients had both

TABLE 19-3. Infectious Complications Following Neuraxial Anesthesia in the Immunocompromised Patient

- The attenuated inflammatory response within the immunocompromised patient may diminish the clinical signs and symptoms often associated with infection and result in a delay in diagnosis and treatment.
- The range of microorganisms causing invasive infection in the immunocompromised host is much broader than that affecting the general population and includes atypical and opportunistic pathogens.
- Initiation of early and effective therapy is paramount in optimizing neurologic outcome – consultation with an infectious disease specialist is advised.
- Prolonged antibiotic therapy (weeks–months) is often required because of persistent and immunologic deficiencies.
- Because eradication of infection is difficult once established, prevention of infection is paramount in caring for immunocompromised patients.

deep track and epidural involvement.) Bacteria cultured were most frequently skin flora. All 19 patients with deep infections were treated with catheter removal and antibiotics; none required surgical decompression or debridement. Catheters were replaced in 15 of the 19 patients who requested them after treatment with no recurrent infections. The authors state recommendations similar to Strafford et al., specifically, long-term epidural catheterization is safe when patients are carefully monitored for signs of infection and receive prompt treatment when the diagnosis is established.

Injection of epidural steroids and underlying disease processes theoretically increase the risk of infection (Figure 19-1).[44–46] Strong[45] described a 71-year-old man with a resolving herpes zoster infection involving the T5-6 dermatome. An epidural catheter was placed at the T6-7 interspace, and 120 mg of methylprednisolone in 5 mL of 0.25% bupivacaine was injected. Three additional doses of bupivacaine were administered, and the catheter was removed intact 26 hours after placement. Four days later, a second epidural catheter was placed at the T5-6 level. Oral antibiotic therapy was initiated. Ten intermittent boluses of 0.25% bupivacaine were made over a 3-day period, and the catheter was then removed. There was no evidence of infection at either catheter insertion site. The patient returned 3 weeks later with a fever, stiff neck, headache, and right-sided flank pain. No neurologic deficits were noted. A thoracic computed tomography (CT) scan revealed an epidural abscess extending from T5-9. An emergency decompressive laminectomy was performed. Cultures at the surgical site were positive for *S. aureus*. The patient was treated with 21 days of intravenous antibiotics, and was discharged without neurologic deficits. Factors contributing to this patient's epidural infection include an immunocompromised host (as suggested by the activation of a latent herpes infection), multiple catheter placement, and decreased immunologic response secondary to steroid administration.

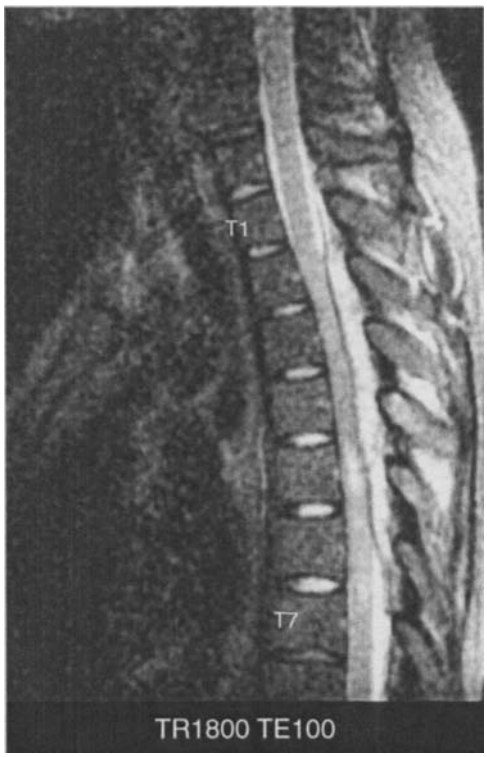

FIGURE 19-1. A thoracic epidural abscess is demonstrated by magnetic resonance image in a patient who underwent thoracic epidural placement for management of herpetic neuralgia. (*Source:* Horlocker TT, Wedel DJ. Regional anesthesia and infection. In: Finucane BT, ed. *Complications of Regional Anesthesia*. Philadelphia: WB Saunders; 1999:170–183. Reprinted with permission from Elsevier.)

Herpes Simplex Virus

HSV type-2 (HSV-2) is an incurable, recurrent disease characterized by asymptomatic periods alternating at variable periods with recrudescence of the genital lesions. The primary infection is associated with viremia and can be accompanied by a variety of symptoms including fever, headache, lymphadenopathy, and, in rare cases, aseptic meningitis. In contrast, recurrent or secondary infections present as genital lesions without evidence of viremia. When obstetric patients present for delivery with evidence of active HSV-2 infection, cesarean delivery is usually recommended to avoid exposing the neonate to the virus during vaginal delivery. The use of central neuronal block has been considered controversial by some because of the theoretical concern of introducing the virus into the CNS. Although this issue is usually discussed in the context of obstetric anesthesia, the incidence and prevalence of genital herpes has increased dramatically in the past two decades. Therefore, the theoretical risk of CNS contamination is present in the general surgical population as well.

Bader et al.[47] reviewed management of 169 HSV-2 – infected patients undergoing cesarean delivery. Five were classified as having primary infections with the remaining 164 being secondary. General (59), spinal (75), and epidural (35) anesthetic techniques were used. One patient with primary HSV-2 developed transient unilateral leg weakness following bupivacaine spinal anesthesia. The problem resolved within 1 week. Although this patient was classified by the obstetrician as having a primary infection, genital lesions had appeared 3 weeks before delivery and there was an active lesion at the time of delivery. The number of patients with primary HSV-2 infections was very small in this study; however, the authors suggested that regional anesthesia was safe in cases of secondary infection.

These recommendations are consistent with previous studies. Crosby et al.[48] reviewed a 6-year experience with active HSV-2 infections in obstetric patients in two institutions. Cesarean delivery was performed on 89 affected parturients, all with recurrent herpes disease. There were no neurologic or infectious complications. In a similar retrospective review, Ramanathan et al.[49] reported 43 epidural anesthetics in parturients with HSV-2 infection who had either active lesions (71%) or had at least one recurrence during the pregnancy. Again, no complications were noted in the parturient or neonate. One patient who was treated prenatally with steroids to promote fetal lung maturity developed a lesion in the postnatal period which resolved within 10 days. Neither of these studies included patients with primary infections.

HSV type-1 (HSV-1), the infectious agent for oral herpes, rarely causes genital lesions. However, recurrent HSV-1 has been described in parturients receiving intrathecal and epidural morphine for pain management.[50] The postnatal association is controversial because several other factors such as emotional or physical stress, other infections, and parturition have been cited as causes of recurrent HSV infection. Valley et al.[51] reported a case of thoracic and labial HSV-1 infection in a patient receiving epidural fentanyl. Although surgical stress may have been a factor, this patient had no other known risk factors, and lesions developed near the site of the epidural catheter.

Human Immunodeficiency Virus

The risk of performing regional anesthesia procedures in HIV-infected patients is largely unknown. Hughes et al.[52] reported the safe administration of central neuronal block in 18 HIV-infected parturients. The patients studied showed no postpartum change in immune, infectious, or neurologic status. Avidan et al.[53] and Bremerich et al.[54] also reported a low complication rate for parturients with HIV infection on antiretroviral therapy who underwent spinal anesthesia. However, in all three series (with a combined total of 117 patients), the patients were relatively healthy and in the early stage of their disease. The effects of anesthesia on patients with more advanced disease are unreported.

In a report on the use of epidural blood patch for postdural puncture headache in HIV-positive males, Tom et al.[55] followed nine patients longitudinally for periods ranging from 6 to 24 months. No complications were attributable to the epidural blood patch, although the authors noted the high incidence of neurologic manifestations in this population. Approximately 40% of patients with the diagnosis of acquired immune deficiency syndrome (AIDS) have clinical signs of neurologic disease and at autopsy, patients with AIDS have a 70%–80% incidence of neuropathologic changes. Although many of the neurologic symptoms are unrelated to complications associated with spinal or epidural anesthesia, some such as aseptic meningitis, chronic headaches, and polyneuropathy may be mistaken for problems related to needle placement. A clear understanding of the association of CNS symptoms with HIV infection is important in order to interpret postblock neurologic pathology.

Aseptic Technique

Although previous publications have repeatedly recommended meticulous aseptic technique, there are no defined standards for asepsis during the performance of regional anesthetic procedures[56] (Table 19-4). Handwashing remains the most crucial component of asepsis; gloves should be regarded as a supplement to – not a replacement for – handwashing.[57] Conversely, the use of gowns and gloves does not further reduce the likelihood of cross-contamination. Surgical masks, initially considered a barrier to protect the *proceduralist* from patient secretions and blood, may be appropriate because of the increasing number of cases of postspinal meningitis, many of which result from contamination of the epidural or intrathecal space with pathogens from the operator's buccal mucosa.[4,20–22] Schneeberger et al.[20] reported four cases of iatrogenic meningitis following spinal anesthesia occurring over a 4-year period. The patients typically presented 24 hours postoperatively with a severe headache (two received an epidural blood patch). All cases involved the same anesthesiologist, who had a history of recurrent pharyngitis and did not wear a mask during the procedure. Interestingly, similar reports have been noted among patients undergoing pain procedures.[58]

Antiseptic Solutions

Controversy still exists regarding the most appropriate and safe antiseptic solution for patients undergoing neuraxial and peripheral techniques. Povidone iodine and chlorhexidine gluconate (with or without the addition of isopropyl alcohol) have been most extensively studied.[59,60] In nearly all clinical investigations, the bactericidal effect of chlorhexidine was more rapid and more effective (extending hours after its application) than povidone iodine. Kinirons et al.[59] compared the rate of epidural colonization using 0.5% chlorhexidine in alcohol with that of 10% povidone iodine. Catheters inserted after skin preparation with chlorhexidine were one-sixth as likely and less quickly colonized as catheters inserted after skin preparation with povidone iodine.

TABLE 19-4. Variables that May Influence Infectious Complications

- Site of catheter placement (thoracic versus lumbar versus caudal)
- Choice of antiseptic and technique of application
- Choice of barrier protection (masks, gloves, gowns)
- Timing and selection of perioperative antibiotics
- Duration of neuraxial or peripheral catheterization
- Use of bacterial filters
- Dressing type(s) (transparent versus dry gauze dressing; use of antiseptic dressings)

Source: Hebl.[56] Reprinted with permission from the American Society of Regional Anesthesia and Pain Medicine.

Although the authors concluded that the use of alcoholic chlorhexidine for cutaneous antisepsis before epidural catheter insertion reduces the risk of catheter colonization, it must be noted that chlorhexidine-alcohol labeling contains a warning against use as a skin preparation before lumbar puncture. Thus, at this time, chlorhexidine is recommended for peripheral and epidural techniques only.

Infectious Complications of Peripheral Regional Techniques

Although meningitis and epidural abscess are the most significant infectious complications of regional anesthesia, the associate risk following plexus and peripheral techniques remain undefined. Auroy et al.[16] reported no infectious complications in 21,278 single-injection peripheral nerve blocks. This low incidence is supported by Borgeat et al.'s[61] report of no complications in 521 patients undergoing interscalene nerve blockade.

The more frequent placement of catheters for peripheral nerve blockade, often for prolonged periods, might be expected to increase the risk of infectious complications; however, few data are available to support this theoretical assumption. Two studies look more specifically at the infectious risk in continuous peripheral nerve blocks. Capdevila et al.[25] prospectively studied 1416 patients in 10 centers undergoing continuous peripheral nerve blocks for orthopedic procedures. A total of 969 (68%) catheters were cultured when removed, and patients were actively monitored for signs of localized infection or sepsis. A positive bacterial colonization was found in 278 (29%) catheters, most frequently *S. epidermidis.* The incidence of local inflammation was present in 3% of patients. In these patients, 44% of the catheters were colonized, whereas only 19% of catheters were colonized in patients without inflammatory signs. There was no correlation between colonization and the presence of fever. Risk factors for local infection/inflammation were admission to an intensive care unit, male gender, catheter duration exceeding 48 hours, and lack of antibiotic prophylaxis. A study by Cuvillon et al.[26] investigated the incidence of infectious complications in 211 continuous femoral catheters. Colonization of the 208 catheters examined after 48 hours showed a rate of 57% with the most common organism again being *S. epidermidis* (71%). Echography was performed in each instance of positive catheter colonization. No cellulitis or abscess was noted; however, three transitory bacteremias were attributed to the presence of the femoral catheters. There were no long-term sequelae attributable to infectious causes. Although the necessity of antibiotic prophylaxis during placement of permanent epidural catheters and implantable devices to treat chronic pain is well defined,[23,62] the importance of antibiotic prophylaxis during placement and maintenance of neuraxial or peripheral catheters is less clear. In a series of 405 axillary catheters, the single infectious complication occurred in a nonsurgical patient who did not receive the "usual" perioperative antibiotic prophylaxis.[63]

Anesthetic Management

These studies and epidemiologic data provide guidance in the administration of spinal or epidural anesthesia in the febrile patient. However, as with all clinical judgments, the decision to perform a regional anesthetic technique must be made on an individual basis considering the anesthetic alternatives, the benefits of regional anesthesia, and the risk of CNS infection (which may theoretically occur in any bacteremic patient).

Numerous clinical and laboratory studies have suggested an association between dural puncture during bacteremia and meningitis. The data are not equivocal, however. The clinical studies are limited to pediatric patients who are historically at high risk for meningitis. Many of the original animal studies used bacterial counts that were

far in excess of those noted in humans in early sepsis, making CNS contamination more likely.[32,64] Despite these conflicting results, it is generally recommended that, except in the most extraordinary circumstances, central neuronal block should not be performed in patients with untreated systemic infection.

Patients with evidence of systemic infection may safely undergo spinal anesthesia, provided appropriate antibiotic therapy is initiated *before* dural puncture, and the patient has demonstrated a response to therapy, such as a decrease in fever.[33,65] Although few data exist on the administration of epidural anesthesia in the patient with a treated systemic or local (distant) infection, the studies by Bader et al.,[11] Goodman et al.,[13] and Darchy et al.[36] are reassuring. Placement of an indwelling epidural (or intrathecal) catheter in this group of patients remains controversial; patients should be carefully selected and monitored for evidence of epidural infection.

Spinal anesthesia may be safely performed in patients at risk for low-grade transient bacteremia after dural puncture. Once again, little information exists concerning the risk of epidural anesthesia in patients suspected of developing an intraoperative transient bacteremia (such as during a urologic procedure). However, short-term epidural catheterization is likely safe, as suggested by large retrospective reviews which included a significant number of obstetric and urologic patients (Table 19-1).

All patients with an established local or systemic infection should be considered at risk for developing infection of the CNS. Patients should be observed carefully for signs of infection when a continuous epidural catheter is left in place for prolonged periods. In addition, injection of local anesthetic or insertion of a catheter in an area at high risk for bacterial contamination such as the sacral hiatus may also increase the risk for abscess formation.[66,67]

Central neuronal block has been shown to be safe in patients with recurrent HSV infections, although exacerbations of HSV-1 have been reported in association with intrathecal and epidural opioids. There are inadequate data available regarding the safety of spinal and epidural anesthesia in the presence of primary HSV-2 infection; however, viremia, fever, and meningitis have been reported. These findings would suggest a conservative approach.[47–50] Minimal data suggest that regional anesthesia can be performed safely in HIV-infected patients, although underlying neurologic pathology is common in these patients.[51–55]

Diagnosis and Treatment

A delay in diagnosis and treatment of major CNS infections of even a few hours significantly worsens neurologic outcome. Bacterial meningitis is a medical emergency. Mortality is approximately 30%, even with antibiotic therapy. Meningitis presents most often with fever, severe headache, altered level of consciousness, and meningismus. The diagnosis is confirmed with a lumbar puncture. Lumbar puncture should not be performed if epidural abscess is suspected, because contamination of the intrathecal space may result. CSF examination in the patient with meningitis reveals leukocytosis, a glucose level of less than 30 mg/dL, and a protein level greater than 150 mg/dL. In addition, the anesthesiologist should consider atypical organisms in patients suspected of meningitis following spinal anesthesia.

Abscess formation following epidural or spinal anesthesia can be superficial, requiring limited surgical drainage and intravenous antibiotics. Superficial infections present with local tissue swelling, erythema, and drainage, often associated with fever, but rarely causing neurologic problems unless untreated. Epidural abscess formation usually presents days to weeks after neural blockade with clinical signs of severe back pain, local tenderness, and fever associated with leukocytosis (Table 19-5). The clinical course of epidural abscess progresses from spinal ache and root pain, to weakness (including bowel and bladder symptoms) and eventually paralysis.[7,8] The initial back pain and radicular symptoms may remain stable for hours to weeks. However,

TABLE 19-5. Differential Diagnosis of Epidural Abscess, Epidural Hemorrhage, and Anterior Spinal Artery Syndrome

	Epidural abscess	Epidural hemorrhage	Anterior spinal artery syndrome
Age of patient	Any age	50% older than 50 years	Elderly
History	Infection or immunosuppression*	Anticoagulants	Arteriosclerosis/ hypotension
Onset	1–3 days	Sudden	Sudden
Generalized symptoms	Fever, malaise, back pain	Sharp, transient back and leg pain	None
Sensory involvement	None or paresthesias	Variable, late	Minor, patchy
Motor involvement	Flaccid paralysis, later spastic	Flaccid paralysis	Flaccid paralysis
Segmental reflexes	Exacerbated,* later obtunded	Abolished	Abolished
Myelogram/CT scan	Signs of extradural compression	Signs of extradural compression	Normal
CSF	Increased white cell count	Normal	Normal

Source: Horlocker TT, Wedel DJ. Regional anesthesia and infection. In: Finucane BT, ed. Complications of Regional Anesthesia. Philadelphia: WB Saunders; 1999:170–183. Reprinted with permission from Elsevier.
*Infrequent findings.

the onset of weakness often progresses to complete paralysis within 24 hours. Radiologic evidence of an epidural mass in the presence of variable neurologic deficit is diagnostic. Magnetic resonance imaging is advocated as the most sensitive modality for evaluation of the spine when infection is suspected.[35,68,69] A combination of antibiotics and surgical drainage remains the treatment of choice. As with spinal hematoma, neurologic recovery is dependent on the duration of the deficit and the severity of neurologic impairment before treatment.[4,5,8]

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