Regional Anesthesia in the Immunocompromised Patient

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Neuraxial anesthesia and analgesia provide several advantages over systemic opioids, including superior analgesia, reduced pulmonary complications, decreased incidence of graft occlusion, and improved joint mobility after major orthopedic surgery.[1-4] In addition, neuraxial analgesia may decrease the risk of infection through attenuation of the stress response and preservation of immune function.[1] Despite these benefits, patients with altered immune status because of diabetes, neoplasm, immunosuppression after solid organ transplantation, and chronic infection with human immunodeficiency virus (HIV) or herpes simplex virus (HSV) are often not considered candidates for neuraxial techniques because of the risk of infection around the spinal cord or within the spinal canal. These patients are susceptible to infection with opportunistic pathogens and because antimicrobial therapy is less effective, experience increased morbidity and mortality compared with patients with normal immune function. Thus, a depressed immune state increases both frequency and severity of infection.

The relative risk of central nervous system (CNS) infections in patients with altered immune status compared with the normal host is unknown. 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.[5-7] However, recent epidemiologic series from Europe suggest that the frequency of infectious complications associated with neuraxial techniques may be increasing.[8,9] In a national study conducted from 1997 to 1998 in Denmark, Wang et al.[9] calculated the risk of persisting neurologic deficits to be 1:4,343 after epidural analgesia. Moen et al.[8] reviewed the Swedish experience from 1990 to 1999 and reported a low incidence of epidural abscess but an alarming association of post–spinal block meningitis. Often these infections occurred in patients with impaired immunity.

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Neuraxial Anesthesia and Analgesia and Immune Function

There are many host defensive mechanisms. The first barrier (or line of defense) is the skin, which supports the importance of aseptic techniques during regional anesthesia. However, once an organism enters the body, 2 distinctly different types of immunologic reaction may occur: humoral and cell mediated. Humoral immunity involves the synthesis and release of antibodies into the blood and other bodily fluids. Antibodies, which are produced by B lymphocytes, neutralize toxins and enhance the phagocytosis of bacteria. Cell-mediated mechanisms confer immunity to those infectious organisms that have developed the capacity to live and multiply within the cells of the host (i.e., viruses, parasites, and mycobacteria). The cell-mediated response uses the actions of T lymphocytes and phagocytes to engulf and destroy viruses, fungi, and cells foreign to the body (including tissue/organ grafts). About 70% of the T lymphocytes are helper/inducer cells that increase the number of macrophages and neutrophils responding to infection. These T lymphocytes also facilitate the production of antibodies by stimulating the growth and function of B lymphocytes. The remaining 30% of T lymphocytes are cytotoxic and directly attack and lyse cells bearing a target antigen. Although there is interaction among the components of the immune system, each immunodeficient state is associated with susceptibility to a subset of pathogens. For example, patients with impaired neutrophil function, such as those with diabetes, are prone to infection with *Staphylococcus aureus* and *Candida*. Infections caused by viruses are more common among

Table 1. Infection 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.

patients with T-lymphocyte deficiency, including patients with HIV and lymphoma.

Experimental models and clinical investigations have consistently shown that the surgical stress response suppresses both cellular and humoral immune function for several days after surgery.[10] Furthermore, the immunosuppressive effects may be exaggerated and/or prolonged in patients with preexisting immunologic dysfunction (Table 1). These effects are clinically significant and result in a predisposition to not only postoperative infection but also tumor growth and metastases.[11,12] For example, the transient suppression of immune function after perioperative blood transfusion significantly increases the frequency of infectious complications and may alter the incidence of disease recurrence in patients with colorectal cancer.[13]

Anesthetic management may theoretically affect perioperative outcome through modification of the inflammatory and endocrine responses to surgical stress.[14] General anesthesia, with the exception of large doses of opioids, does not suppress the surgical stress response and thus may exacerbate postoperative immunosuppression.[15] Conversely, neuraxial anesthesia and analgesia, is associated with a modest preservation of cellular and humoral immune function. The effects are most pronounced for high-risk patients undergoing procedures below the umbilicus.[1] The attenuation of the stress response associated with regional techniques is maintained in the presence of a combination general-neuraxial anesthetic, provided that epidural analgesia is continued into the postoperative period; single-injection spinal and epidural techniques do not substantially modify postoperative impairment of immune function. The effect of peripheral blockade on the stress response/immune function remains undetermined.

In summary, despite these documented benefits, the clinical importance of anesthesia-mediated changes in perioperative immunosuppression remains uncertain. Currently, there are no clinical studies evaluating the influence of choice of anesthesia and analgesia on outcome after oncologic surgery or in immunocompromised patients.

Epidemiology and Pathogenesis 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 after the introduction and increasingly widespread use of vaccines for *H influenzae* and *N meningitides*. Currently, *Staphylococcus pneumoniae* accounts for nearly two thirds of community acquired meningitis; causative organisms of nosocomial meningitis include gram-negative bacilli, *S aureus*, and coagulase-negative staphylococci. Most cases of meningitis are associated with a recent infection (particularly otic or respiratory) or head trauma. Additional risk factors include altered immune states, including infection with HIV, a history of intravenous drug use/abuse, or recent head trauma.

Patients with acute bacterial meningitis may deteriorate rapidly. The duration of symptoms before presentation is often less than 24 hours. The classic triad of fever, nuchal rigidity, and altered mental status may not be present in one third of patients. Bacterial meningitis is a medical emergency; mortality is 100% if untreated. Even with appropriate antibiotic therapy, mortality remains at approximately 30%. The diagnosis is confirmed with a lumbar puncture. Blood cultures should also be performed. Lumbar puncture should not be performed if epidural abscess is suspected because contamination of the intrathecal space may result. Atypical organisms, particularly those associated with the specific immunologic deficiency, should be considered.[16] Of paramount importance is the immediate institution of antibiotic therapy that is bactericidal for the organism as well as associated with a high penetration across the blood-brain barrier.

Epidural abscess accounts for 2 to 12 cases per 100,000 admissions to tertiary hospitals.[6] Significant risk factors include compromised immunity (diabetes mellitus, malignancy, steroid use, and HIV infection) and instrumentation of the vertebral column (trauma, surgery, diskography, and neuraxial

block). The source of the infection is contiguous soft tissue/skin or bone and hematogenous spread from a respiratory or urinary source to the epidural space.[7] Most infections are bacterial, although mycobacterial and fungal abscesses may occur. The most commonly identified organisms are *S aureus* (57%), streptococci (18%), and gram-negative bacilli (13%).[6,17]

Abscess formation after epidural or spinal anesthesia can be superficial, requiring limited surgical drainage and intravenous antibiotics only. Superficial infections present with local tissue swelling, erythema, and drainage, often associated with fever but rarely causing neurologic problems unless untreated. Diagnosis may be more difficult and is often delayed in patients with chronic epidural abscesses because these patients are less likely to be febrile or have an elevated leukocyte count compared with patients with acute abscesses. The clinical course of epidural abscess progresses from spinal ache and root pain to weakness (including bowel and bladder symptoms) and eventually paralysis.[18,19] The initial back pain and radicular symptoms may remain stable for hours to weeks. However, 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.[20-22] Surgical drainage is performed in the presence of severe and/or rapidly progressing neurodeficits. Steroid administration and increased neurologic impairment at the time of surgery adversely affects outcome. Early diagnosis and intervention is crucial; complete recovery is reported in less than 40% of cases and typically occurs in patients with symptoms for less than 36 hours.[8,9,17,19]

Meningitis and Epidural Abscess After Neuraxial Block

Neuraxial anesthesia is a rare etiology of CNS infections.[8,9] Aromaa et al.[23] reported 8 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 recent epidemiologic series are alarming. In a national study conducted from 1997 to 1998 in Denmark, Wang et al.[9] reported the incidence of epidural abscess after epidural analgesia was 1:1,930 catheters. Eight of 9 patients with epidural abscess were immunocompromised (cancer, diabetes, and trauma). In addition, patients with epidural abscess had an extended duration of epidural catheterization (median 6 days, range 3-31 days). Often the diagnosis was delayed; the time to 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). This series confirmed the conjecture of previous single case reports that epidural abscess is more likely to occur in immunocompromised patients and that prolonged duration of epidural catheterization increases the risk of epidural abscess.

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.[8] reported 42 serious infectious complications. Epidural abscess occurred in 13 patients; 9 (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). Prevailing symptoms were fever and severe backache; 5 developed neurologic deficits. All 7 positive cultures isolated *S aureus*. Overall, neurologic recovery was complete in 7 of 12 patients. However, 4 of the 5 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 after 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 1. Meningitis resulted in residual neurologic deficits in 6 patients.

These large epidemiologic studies represent new and unexpected findings regarding the demographics, frequency, etiology, and prognosis of infectious complications after 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 after neuraxial blockade typically are healthy and have undergone uneventful spinal anesthesia. The organism is often cultured from the oropharynx of the proceduralist, implying an iatrogenic etiology.[8,24] However, with few exceptions, large series and cases reporting oropharyngeal flora as the pathogen in post–spinal meningitis have been European in origin.[24] Likewise, this trend has not been reported with respect to meningitis after diagnostic lumbar puncture.[25] Although the frequency of serious infectious complications is much higher than reported previously, the results may be because of differences in reporting and/or clinical practice (asepsis, perioperative antibiotic therapy, duration of epidural catheterization, and patient selection).[8,9] 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.[26-29]

Neuraxial Block in the Immunocompromised Patient

Large series have shown that patients with immunodeficiencies are at increased risk for infectious complications compared with those with intact immune function.[8,9] However, there are few investigations that have evaluated the frequency of meningitis or epidural abscess within a specific immunodeficient population. Strafford et al.[30] reviewed 1,620 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 to spine, chest wall, and lungs became febrile after 10 days of epidural catheterization. The catheter was removed; culture showed 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 *C tropicalis* was present in the epidural space. Her neurologic deficits resolved postoperatively. Three additional patients with chronic pain syndromes were evaluated for epidural infection; 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.[31] studied 350 cancer and HIV-infected patients in whom permanent (tunneled) epidural catheters were placed. The authors examined 3 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 1 in every 1,702 days of catheter use in the 19 patients who developed deep-track (n = 8) or epidural (n = 15) infections. (Four of the 19 patients had both 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 (Fig 1).[32-34] Strong[33] described a 71-year-old man with a resolving herpes zoster infection involving the T5-T6 dermatome. An epidural catheter was placed at the T6-T7 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-T6 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 scan revealed an epidural abscess extending from T5-T9. 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.

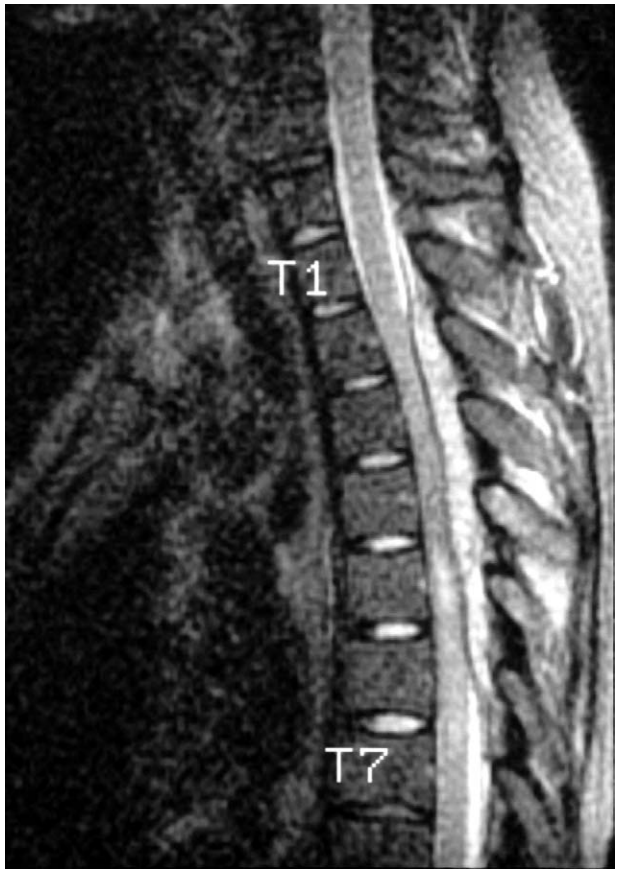

Fig 1. A thoracic epidural abscess is shown by magnetic resonance image in a patient who underwent thoracic epidural placement for management of herpetic neuralgia. (Reprinted with permission from Horlocker TT, Wedel DJ. Regional anesthesia and infection. In: Finucane BT, ed. Complications of Regional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

Herpes Simplex Virus

Herpes simplex virus type 2 (HSV-2) is an incurable, recurrent disease characterized by asymptomatic periods alternating at variable periods with recrudescence of the genital lesions.[35] 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 section is usually recommended to avoid exposing the neonate to the virus during vaginal delivery.[35] 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 obstetrical anesthesia, the incidence and prevalence of genital herpes has increased dramatically in the past 2 decades. Therefore, the theoretical risk of CNS contamination is present in the general surgical population as well.

Bader et al.[36] 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 (n = 59), spinal (n = 75), and epidural (n = 35) anesthetic techniques were used. One patient with primary HSV-2 developed transient unilateral leg weakness after 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 those of previous studies. Crosby et al.[37] reviewed a 6-year experience with active HSV-2 infections in obstetrical patients in 2 institutions. Cesarean section was performed on 89 affected parturients, all with recurrent (and active) herpes disease. There were no neurologic or infectious complications. In a similar retrospective review, Ramanathan et al.[38] reported 43 epidural anesthetics in parturients with HSV-2 infection who had either active lesions (71%) or had at least 1 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. These limited results suggest that neuraxial block in patients with recurrent disease appears safe. However, the risk of CNS contamination during a primary infection, where the likelihood of spontaneous CNS infection may occur (although rarely) and viremia is relatively common, remains undetermined.

Herpes simplex virus 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.[39] 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.[40] reported a case of thoracic and labial HSV-1 infec-

tion 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. The mechanism of reactivation of HSV remains speculative.

HIV

The risk of performing regional anesthesia procedures in HIV-infected patients is largely unknown. Involvement of the CNS occurs within the first weeks or months in the course of HIV infection. Thus, introduction of the virus into the subarachnoid space during spinal anesthesia is not of concern. However, clinicians must maintain a clear understanding of the association of neurologic disorders during HIV infection in order to interpret post-block neurologic pathology. For example, approximately 90% of patients with HIV infection have neuropathologic abnormalities present at autopsy, and clinical symptoms are reported by 30% to 95% of patients in late stages of the infection.[41] 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. In addition, opportunistic infections may also contribute to both central and peripheral neural dysfunction (Table 2). Finally, retroviral medications (stavudine and didanosine) are also associated with neurotoxicity.[41] Overall, these patients are at increased risk of perioperative worsening of neurologic deficits because of the combined effects of the underlying viral and opportunistic infections, therapy, regional anesthesia, surgery, and positioning.

There are sparse data quantifying the risk of neurologic or infectious complications among patients with HIV infection. All have involved patients early in the disease with relatively stable immune status. Hughes et al.[42] 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.[43] and Bremerich et al.[44] also reported a low complication rate for parturients with HIV infection on antiretroviral therapy who underwent spinal anesthesia. However, in all 3 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.[45] followed 9 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.

Table 2. Neurologic Complications of Human Immunodeficiency Virus (HIV) Infection

HIV-Related Disorders Without Opportunistic Etiologies	HIV-Related Disorders With Opportunistic Etiologies
Aseptic meningitis	Cryptococcal meningitis
HIV encephalopathy	Cytomegalovirus meningitis
Inflammatory demyelinating polyneuropathy	Herpes encephalitis
Mononeuritis multiplex	Lymphoma (central nervous system)
Myopathy	Progressive multifocal leukoencephalopathy

Noninfectious Complications of Regional Block in the Immunocompromised Patient

Comorbidities related to the immunocompromised patient's underlying condition may increase the risk of neurologic and hemorrhagic complications after neuraxial or peripheral techniques. The clinician must therefore be aware of associated changes in hemostasis, likelihood of bony metastases (particularly to the spine), and the side effects of chemotherapeutic agents.

Hemorrhagic Complications

Hemorrhage can occur whenever any of the components of the coagulation cascade are sufficiently compromised. Because many conditions associated with depressed immune status have abnormalities in production or consumption of platelets and clotting factors, these patients are at risk for not only infectious but also hemorrhagic complications.

Bacterial and viral infection (thrombocytopenia and disseminated intravascular coagulopathy). Thrombocytopenia is the most common effect disorder of hemostasis in the infected patient. Both gram-positive and gram-negative pathogens have been implicated. Although the degree of thrombocytopenia is typically not severe, in 1 series, nearly one third of pediatric patients with septicemia had platelet counts of less than 50,000/μL.[46] The actual etiology of thrombocytopenia during infection is unknown. Proposed mechanisms include bone marrow suppression, splenomegaly (sequestration), bacterial endotoxin, direct bacterial (or viral) damage, and immunologic mechanisms (antibodies directed against bacteria or viruses adhere to platelets, resulting in destruction). Importantly, anti-in-

fectious agents may also result in thrombocytopenia through bone marrow suppression or immunologic destruction.[47] Assessment of a platelet count is advised in patients with purpura or petechiae because these represent significant impairment of hemostasis. Patients with severe (systemic) infections may also develop disseminated intravascular coagulopathy (DIC). However, most patients with laboratory tests consistent with DIC do not have evidence of clinically significant bleeding. The decision to perform a regional anesthetic in the presence of an untreated infection has been extensively discussed.[24] Because these patients are at risk for significant infectious or hemorrhagic complications, neuraxial technique should not be performed, except in extraordinary circumstances.

Neoplasm (hemorrhagic and thromboembolic disorders). The hemostatic abnormalities associated with cancer are diverse and variable; every component of the hemostatic mechanism is potentially affected (Table 3). Patients with neoplasm may spontaneously develop thromboembolic or hemorrhagic complications. These events are associated with laboratory evidence of DIC and are present in 50% of patients with cancer and 90% of patients with metastatic disease.[48] However, clinical manifestations occur less frequently. Overall, in patients with solid tumors, thromboembolic events are most common, whereas hemorrhage occurs more often in patients with acute leukemia. Thus, cancer patients may exist along a spectrum of coagulability ranging from hypercoagulable to fibrinolytic.

Quantitative and qualitative platelet abnormalities are often present in the cancer patient. Thrombocytopenia, from decreased production, increased destruction, or sequestration of platelets, is the single most common cause of bleeding in cancer patients. Bone marrow suppression from chemotherapy or radiation and decreased production because of bone marrow involvement or nutritional deficiencies are leading etiologies of quantitative platelet abnormalities among this patient population. Conversely, qualitative abnormalities of platelet function, including reduced adhesion, abnormalities of aggregation, and poor clot retraction are common among patients with myeloproliferative disorders. In these patients, the risk of hemorrhagic complications is not correlated with platelet count, but the results of special adherence assays. Platelet transfusions are rarely required; however, the additive effects of antiplatelet medications and anticoagulants should be considered in patients with quantitative or qualitative platelet dysfunction. Production and inhibition of one or more clotting factors may also be directly affected by cancer, particularly primary or metastatic liver cancer, multiple myeloma, and other malignant paraprotein disorders. A targeted evaluation of the hemostatic mechanism is warranted for patients with a history of recent chemotherapy or a myeloproliferative disorder.[49] The decision to proceed with neuraxial or noncompressible peripheral techniques in patients is based on the degree and character of the coagulation dysfunction, the presence of alternative anesthetic or analgesic methods, and the anticipated length of therapy. For example, cancer patients near the end of life may experience severe pain that is untreated by systemic opioids. Short-term (nonpermanent) epidural catheterization may be warranted in selected cases, despite the presence of thrombocytopenia and/or neutropenia.[29] However, the decision should be made on an individual basis, weighing the relative risks and benefits.

Special consideration must be given before performing neuraxial block, diagnostic lumbar puncture, and epidural blood patch in patients with acute lymphoblastic leukemia (ALL). Traumatic or bloody puncture of the dura may worsen outcome by seeding the CNS with blast cells.[50] Therefore, among ALL patients with circulating leukemic cells, it has been recommended a platelet count of 100,000/μL be achieved (through platelet transfusion, if necessary) before diagnostic lumbar puncture.[50] Interestingly, oncologists seldom recommend platelet transfusion to avoid spinal hematoma unless the platelet count is less than 10,000/μL, although the transfusion trigger remains controversial.[50,51] There were no spinal hematomas in a series of 5,609 lumbar punctures performed in children with ALL, including 1,009 patient with had platelet counts $<$50,000/μL.[50] Extrapolating these recommendations (from both hemorrhagic and oncologic per-

Table 3. Hemostatic Disorders in Cancer Patients

Hemostatic Disorder	Neoplasia
Intravascular disseminated coagulation and fibrinolysis (DIC)	All neoplasms, related to tumor mass (increased with metastatic disease)
Impaired plasma coagulation	
Organ failure	Hepatic malignancy
Factor inhibitors	Colon, prostate lung cancer
Factor deficiencies	Leukemias (V, VIII, XII, XIII), multiple myeloma (X), malignant melanoma (XI), polycythemia vera (V)
Platelet abnormalities	
Thrombocytopenia	Chemotherapy, tumor invasion, nutritional deficiencies
Thrombocytosis	Myeloproliferative disorders
Qualitative defects	Myeloproliferative disorders

spectives) to neuraxial techniques is problematic. However, because alternative anesthetic techniques exist, it would appear prudent to avoid neuraxial block and epidural blood patch among patients with known circulating leukemic cells. Consultation with the patient's hematologist/oncologist to determine the relative risks and benefits may be helpful.

Acute decompensated DIC is associated with thrombocytopenia; hypofibrinogenemia; prolonged prothrombin, thrombin, and activated partial thromboplastin times; and elevated levels of fibrinogen degradation products. These patients are at high risk for spontaneous or anesthesia-related spinal hematoma and are considered poor candidates for neuraxial blockade.[52] However, patients with less fulminant (chronic/compensated) forms of DIC show less severe abnormalities in standard clotting tests, and values may actually be within "normal" ranges. Rather, these patients are more likely to be prothrombotic. Patients with cancer have a 6-fold risk of developing thromboembolism and may receive pharmacologic prophylaxis with either standard heparin, low–molecular-weight heparin, or warfarin.[53] Because the risk will be further increased in the perioperative period, aggressive thromboprophylaxis is warranted. Anesthetic management is based on the anticoagulant, dosing regimen, and timing of initiation of thromboprophylaxis.[52]

Neurologic Complications

Immunocompromised patients often present with preexisting neurologic dysfunction caused by their primary disease process (spinal cord compression from vertebral column neoplasm, peripheral neuropathy associated with HIV, or diabetes) or as a result of treatment. Based on the "double crush" theory, which hypothesizes that axons injured at 1 site may be particularly susceptible to damage,[54] these patients may be at increased risk for neurologic complications of regional anesthesia. Furthermore, the damage of the dual injury exceeds the expected additive damage caused by each isolated injury.[52] Thus, the effects of needle trauma, ischemia, and local anesthetic toxicity are exaggerated and a relatively minor injury applied to a previously dysfunctional nerve may result in new (or exacerbation of existing) symptoms.[54,55]

Vertebral column metastases. Although any tumor may involve bone, the most common are metastatic cancer of the breast, lung, prostate, and multiple myeloma. Frequent sites of bony metastasis are the vertebral column, skull, humerus, ribs, pelvis, and femur. Patients often present with pending or existing pathologic fractures requiring surgical fixation. Although these procedures may be performed under neuraxial blockade, the presence of vertebral column metastases/spinal cord compression must first be considered.

The vertebral column, particularly the thoracic spine, is the most common site of bony metastasis; 98% of known cancer patients who present with back pain have underlying metastases. For example, vertebral metastases in patients with a known primary tumor have been described in 90% of patients with prostate cancer, 74% with breast cancer, 45% with lung cancer, 29% with lymphoma or renal cell carcinoma, and 25% with gastrointestinal cancers. Vertebral column involvement is not an absolute contraindication to neuraxial block. However, patients with extension into the epidural space may develop spinal cord compression; the 3 most common cancers associated with extradural compression are prostate, breast, and lung.[56]

Because back pain in patients with cancer usually signifies bone or epidural metastasis, investigation to define the presence and extent of tumor involvement is necessary before performance of a neuraxial technique. The evaluation of a patient with back pain depends on whether there has been a recent change in the back pain or any evidence of neurologic compromise. Evaluation of stable back pain without neurologic deficits is not urgent and includes plain radiographs of the affected area. Conversely, rapidly progressing back pain in a patient with cancer is highly suspicious for epidural tumor or fracture and should be investigated with either magnetic resonance imaging or computed tomography myelography within 24 hours. Increased pain in the supine or erect position and radiating pain indicate potential cord or root impingement. Loss of motor function, hyperreflexia or hyporeflexia, or bowel/bladder dysfunction are suggestive of myelopathy and necessitate immediate intervention to prevent permanent neurologic deficits.[56] Thorough review of spine imaging studies and neurologic examination is essential in the anesthetic management of cancer patients with back pain.

Neuropathy after anticancer therapy. Neurologic complications of anticancer therapy may result from direct toxic effects on the nervous system or indirectly from drug-induced metabolic derangements. Although a variety of neuropathic conditions may arise after chemotherapy with cisplatin, suramin, taxanes (paclitaxel and docetaxel), or vinca alkaloids, peripheral neuropathy is the most common. Both demyelination and axonal loss may occur. Patients typically present with paresthesias, numbness, and occasionally weakness of the fingers and toes that progresses proximally.[57] The frequency

Table 4. Chemotherapeutic Medications Associated With Peripheral Neuropathy

Agent	Percent of Patients Affected	Cumulative Dose Associated With Neuropathy	Clinical Presentation
Cisplatin	85%	300 mg/m^2	Paresthesia, decreased vibratory sense; onset and/or progression for up to 4 months after discontinuation
Suramin	10%	350 μg/mL (concentration dependent)	Both demyelinating (Guillain-Barre) and severe sensorimotor peripheral neuropathy reported
Paclitaxel	60%	250 mg/m^2	Predominately sensory
Docetaxel	10%	500 mg/m^2	Predominately sensory
Vincristine	100% (10-20% with other vinca alkaloids)	May occur with first dose	Sensory and motor

and severity vary between chemotherapeutic agents. Vincristine is the most neurotoxic, with nearly 100% of patients undergoing vincristine chemotherapy developing a peripheral neuropathy. The absence of clinical signs or symptoms does not indicate lack of nerve injury; neurophysiologic testing often shows abnormalities even in the absence of clinical findings, suggesting a subclinical neuropathy is common. In addition, the neuropathy may develop and/or progress for several months after discontinuation of the agent. Therefore, clinicians are encouraged to carefully assess the risks and benefits of performing regional anesthetic techniques in patients with a recent history of chemotherapy, particularly if the cumulative dose has exceeded those reported in Table 4.

Infectious Complications of Peripheral Block in the Immunocompromised Patient

Infections of the CNS may result in paralysis or death. Only recently have the frequency and risk factors associated with meningitis and epidural abscess been determined. However, the frequency, diagnosis, and prognosis of infectious complications after peripheral block remain unclear. Several large series involving continuous plexus and peripheral techniques have reported a high incidence of colonization (20%-60%)[27,28] but few significant infections. To date, there are 3 serious infectious complications of peripheral block. Two of the 3 occurred in immunocompromised patients. Nseir et al.[58] reported a case of fatal necrotizing fasciitis after single-injection axillary block. The 74-year-old woman with a history of diabetes mellitus presented 4 days postoperatively with axillary pain, erythema, and swelling localized to the site of needle placement. Blood and tissue cultures yielded Group A streptococcus. The source of the infection was the patient's skin or proceduralist's oral pharynx. Adam et al.[59] described a psoas abscess complicating femoral catheterization (96 hours) in a healthy 35-year-old woman. Cultures identified *S aureus*. The patient was successfully treated with a 1-month course of antibiotics. Capdevila et al.[27] noted 1 psoas abscess and cellulites among 1,416 continuous regional techniques in a diabetic woman after femoral catheter placement. Catheter culture reported *S aureus*; the patient was treated with antibiotic therapy. The authors also identified intensive care unit admission, peripheral nerve catheterization greater than 48 hours, male gender, and the absence of perioperative antibiotic prophylaxis as risk factors for local infection/inflammation. Although it is not appropriate to develop recommendations based on a limited number of case reports and 2 observational series, it is interesting to note that the apparent risk factors and pathogens for infectious complications of peripheral techniques are strikingly similar to those of neuraxial block.

Anesthetic Management

It is important to note that although the following statements are based on a thorough evaluation of the available information, in some cases data are sparse. Epidemiologic series have documented the safety of neuraxial anesthesia and analgesia in the immunocompromised patient. Unfortunately, with complications as rare as epidural abscess and meningitis, no clinical study to date has sufficient power to definitively determine patient management. Variances from recommendations contained in this document may be acceptable based on the judgment of the responsible anesthesiologist. The consensus statements are designed to encourage safe and quality patient care but cannot guarantee a specific outcome. They are also subject to timely revision as justified by evolution of information and practice. Finally, the current information focuses on neuraxial blocks and infection; the risk after plexus and peripheral techniques remains undefined. Additional experience is needed to allow statements for nonneuraxial blocks.

Recommendations

Recommendations are as follows:

1. Clinical series 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 theoretically are more likely to occur in the immunocompromised patient), as well as the risk of hemorrhagic or neurologic complications (Grade C).
2. The attenuated inflammatory response within the immunocompromised patient may diminish the clinical signs and symptoms often associated with infection. Likewise, 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. Consultation with an infectious disease specialist is advised to facilitate initiation of early and effective therapy (Grade B).
3. A delay in the diagnosis and treatment of CNS infections worsens neurologic outcome and increases mortality (Grade B).
4. The risk of epidural abscess increases with the duration of epidural catheterization (Grade B).
5. 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 (Grade C).
6. 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 (Grade B).
7. Minimal data suggest that neuraxial and peripheral techniques (including epidural blood patch) can be performed safely in HIV-infected patients. The presence of preexisting neurologic pathology is common in these patients and must be considered (Grade C).

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