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The Neurostimulation Appropriateness Consensus Committee (NACC) Recommendations for Infection Prevention and Management

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Introduction: The use of neurostimulation for pain has been an established therapy for many decades and is a major tool in the arsenal to treat neuropathic pain syndromes. Level I evidence has recently been presented to substantiate the therapy, but this is balanced against the risk of complications of an interventional technique.

Methods: The Neurostimulation Appropriateness Consensus Committee (NACC) of the International Neuromodulation Society convened an international panel of well published and diverse physicians to examine the best practices for infection mitigation and management in patients undergoing neurostimulation. The NACC recommendations are based on evidence scoring and peer-reviewed literature. Where evidence is lacking the panel added expert opinion to establish recommendations.

Results: The NACC has made recommendations to improve care by reducing infection and managing this complication when it occurs. These evidence-based recommendations should be considered best practices in the clinical implantation of neurostimulation devices.

Conclusion: Adhering to established standards can improve patient care and reduce the morbidity and mortality of infectious complications in patients receiving neurostimulation.

Keywords: Complications, neuromodulation, perioperative medicine, recommendations, risk reduction, spinal cord stimulation, surgical site infection

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INTRODUCTION

Surgical site infections (SSIs) are linked with significant individual and societal consequences, including morbidity, mortality, and expanding healthcare costs. From an individual standpoint the morbidity may be significant, including additional disability and even a very small risk of death. If a stimulator is explanted because of infection and cannot be appropriately replaced, the patient may be denied the only effective therapy. SSIs related to an implantable device are defined as an infection in the region of an implantable device within one year postoperatively. In the United States and England, SSIs are the second and third most reported healthcare-associated infections, respectively (1,2). In the United States, approximately 500,000 SSIs (17% of all healthcare-associated infections) occur annually and are associated with healthcare-related costs of approximately $10 billion dollars annually (2,3). The Institute for Healthcare Improvement reports that SSIs in the United States increased the length of hospital stay by an average of 7.5 days. In 2013, in the United Kingdom, SSIs accounted for 16% of healthcare-associated infections, resulting in additional costs of between £2,100 and £10,500 per patient, depending on the severity of the infection (4). In general, direct expenses associated with an SSI result in a doubling of total medical inpatient costs. In the modern era of cost containment, even a modest reduction in this potentially devastating problem would have huge implications. It is the goal of the Neurostimulation Appropriateness Consensus Committee (NACC) to provide best practice guidance in this important area.

Recently, significant attention has focused on the occurrence of SSIs and on methods to reduce them. Although defined infection-control recommendations exist from the U.S. Centers for Disease Control and Prevention (CDC) (5), National Institute for Health and Care Excellence (NICE) in the United Kingdom (6), and Surgical Care Improvement Project (SCIP) (7,8), SSI rates have not significantly declined (9). In addition, a recent analysis of the United States Anesthesia Closed Claims Project data base was performed, examining the injury and liability of advanced implantable pain care therapies from 1990 to 2013 (10). Spinal cord stimulation (SCS) and intrathecal (IT) therapy were identified in the 148 device-related claims. Interestingly, the closed claims analysis for both groups indicated that infection continues to be a source for morbidity, as it was the most common damaging event (defined as the mechanism for which the presumed or actual injury occurred) for surgical device-related claims, representing 23% of claims. Furthermore, seven of the 25 identified infections were related to intended or unintended retention of foreign bodies (e.g., sponges, SCS leads).

Efforts to promote the prevention and reduction of SSIs are critical to the advancement of the field of neuromodulation, as appropriate implementation of the therapy is essential to its success. Reported rates of neuraxial and peripheral nerve stimulation techniques are shown in Table 1. Infection rates for SCS have reportedly ranged from 1 to 10% (Table 1), with two large systematic reviews reporting infection rates of 3.4 to 4.6% (11–13). Reported infection rates associated with SCS are often higher than those reported with other implantable devices, including pacemakers and total joint replacement prostheses, indicating the need for additional education and the introduction of best practices for patient selection, surgical technique, and tissue management (14). A recent international survey of 506 physicians conducted to understand the infection-control practices for SCS further highlighted the need for education of physicians performing neuromodulation procedures (15). The survey demonstrated low compliance rates for infection-control recommendations made by the CDC (Table 2), NICE, and SCIP, with only four of 15 recommended practices having compliance rates of $\geq$80% (utilization of perioperative antibiotics for trials and implants, appropriate timing for antibiotic administration, and postoperative application of an occlusive dressing) (15). Areas associated with high levels of noncompliance included weight-based antibiotic dosing, hair removal strategies, double gloving, surgical dressing, skin antiseptic agent selection, and postoperative continuation of antibiotics.

The purpose of this report is to discuss infection-control practices for neuromodulation and describe best practices based on available supporting literature and guidelines, in line with the regularly updated, living documents prepared by the NACC. This report mainly

Table 1. Reported Infections Rates (%) for Neuromodulation-Based Techniques, Including Spinal Cord Stimulation, Dorsal Root Ganglion Stimulation, Sacral Nerve Stimulation, Occipital Nerve Stimulation, Peripheral Nerve Stimulation, and Peripheral Nerve Field Stimulation (Publications Arranged Chronologically Beginning with Most Recent in Each Category).

Publication/type of study/period of follow-up	Therapy type	*N*	Infection rate (%)
Spinal cord stimulation			
Hayek et al. (16) Retrospective review; 12–44.5 months	SCS	234 of 345 implanted	4.3
Al-Kaisy et al. (17) Prospective, multicentre study; 24 months	HF-10 SCS	72	6
Van Buyten et al. (18) Prospective, multicentre European study; 6 months	HF-10 SCS	72	4.8
Engle et al. (19) Retrospective study in cancer pain patients	SCS	59	3.4
Mekhail et al. (20) Retrospective analysis; consecutive patients 2000–2005	SCS	527 of 707 implanted	4.5
Kemler et al. (21) RCT	SCS (CRPS)	24	4
Kumar et al. (22) RCT; 24 months	SCS	42	10
Taylor et al. (23) Systematic review; 2 years post-intervention	SCS (CRPS)	554	4
Kumar et al. (24) Retrospective analysis; 22-year experience	SCS	410	3.4
Taylor et al. (25) Systematic review; 1–120 months	SCS (FBSS)	3427	6
North et al. (26) RCT; up to 3 years postimplantation	SCS	45	6
Turner (12) Systematic review; mean follow-up 1–60 months	SCS	830	4.6
Dorsal root ganglion stimulation			
Liem et al. (27) Prospective, multicentre; 12 months	DRG	51	8.5
Peripheral nerve stimulation			
Deer et al. (28) Prospective, multicenter, randomized, double-blind, partial crossover; 1 year	PNS	45	0 SAEs related to study treatment; AEs were similar in nature for PNS and control group
Saper et al. (29) RCT; 3 months	ONS	51	4 (pocket infection) 14 (lead/extension tract infection)
Paemeleire et al. (30) Retrospective analysis; 1 month minimum	ONS	44	4.5
Peripheral nerve field stimulation			
Sator-Katzenschlager et al. (31) Multicenter, retrospective analysis;	PNfS	111	6
Verrills et al. (32) Retrospective analysis of 100 consecutive patients; 1–23 months	PNfS	100	1
Sacral nerve stimulation			
Brazzelli et al. (33) Systematic review of lit from 1966 to May 2003	SNS	NR	5

SCS, spinal cord stimulation; DRG, dorsal root ganglion; CRPS, complex regional pain syndrome; FBSS, failed back surgery syndrome; SNS, sacral neurostimulation; ONS, occipital nerve stimulation; PNfS, peripheral nerve field stimulation; PNS, peripheral nerve stimulation; RCT, randomized controlled trial; SAE, serious adverse event; AE, adverse event; NR, not reported.

focuses on neuraxial and peripheral neuromodulation systems, while limiting specific discussion of SSIs associated with intracranial procedures. Many of the infection-control practices recommended in this report would also pertain to intracranial devices. When possible, best practices were taken from neuromodulation-specific research, although, since the research is limited, best practices were also

Table 2. Infection-Control Measures Recommended by the Centers for Disease Control and Prevention (5).

Recommendations	Evidence rankings*
Preoperative measures	
Optimize glucose control	IB
Discontinue tobacco use	IB
If hair is removed, use electric clippers immediately before surgery	IA
Use prophylactic antibiotic therapy	IA
Vancomycin should not be used routinely	IB
Intraoperative measures	
Use appropriate preparation technique and agent selection for skin antisepsis	IB
Maintain positive pressure ventilation in the operating room (OR)	IB
Keep the OR doors closed during procedure	IB
Limit OR traffic	II
Handle tissue gently and eradicate dead space	IB
Postoperative measures	
Use occlusive sterile dressing for 4–48 hours postoperatively	IB
If a dressing change is required, use:	
Hand washing	IB
Sterile technique	II

*CDC rankings. IA: Strongly recommended for implementation and supported by well-designed experimental, clinical, or epidemiological studies. IB: Strongly recommended for implementation and supported by some experimental, clinical, or epidemiological studies and strong theoretical rationale. II: Suggested for implementation and supported by suggestive clinical or epidemiological studies or theoretical rationale.

extrapolated from other surgical specialties, and from the clinical expertise of the NACC members. It is imperative that implanting physicians understand the risks for SSIs, their causes, methods to decrease the rate of occurrence, and appropriate identification and management of SSIs.

METHODS

Development Process

The International Neuromodulation Society (INS) strives to improve patient care and access to advanced pain care to relieve suffering caused by disease processes. In order to achieve these goals, the INS created a process for evaluating the level of current evidence in the peer-reviewed literature for issues identified as critical for improving efficacy and safety. In 2012, the INS convened the NACC to study neurostimulation practices, culminating with the first published guidelines in 2014 (11,34–36). Those papers sought to provide wide-ranging insight regarding the entire field of neurostimulation. In 2014, the NACC met again to determine the best practices for specific issues pertinent to neurostimulation. The recommendations contained herein address infection prevention and management for implantable neurostimulation devices.

Literature Search Methods

A literature search was conducted to identify publications relevant to infection management available since the previous NACC publications in 2014. MEDLINE®, BioMed Central®, Current Contents Connect®, Embase®, International Pharmaceutical Abstracts®, and Web of Science®, Google Scholar, and Pubmed data bases were searched from 1959 to July 2016. Authors also performed independent literature searches and compiled evidence for analysis and consensus review. After reviewing the literature, the NACC panel developed recommendations for infection prevention and management.

Evidence Ranking and Consensus Development

As in previous NACC recommendations, the current recommendations use The United States Preventative Services Task Force hierarchies of studies and degrees of recommendations based on evidence rankings as outlined in Tables 3 and 4 (37).

Authors of this manuscript were asked to complete reference forms for their section's assessment. These forms were then reviewed and averaged by the executive committee of the working group. The compiled results served as the basis for review and consensus development. The working group developed recommendations based on

Table 3. Hierarchy of Studies by the Type of Design (U.S. Preventive Services Task Force, Ref [37]).

Evidence level	Study type
I	At least one controlled and randomized clinical trial, properly designed
II-1	Well-designed, controlled, nonrandomized clinical trials
II-2	Cohort or case studies and well-designed controls, preferably multicenter
II-3	Multiple series compared over time, with or without intervention, and surprising results in noncontrolled experiences
III	Clinical experience-based opinions, descriptive studies, clinical observations or reports of expert committees.

Table 4. Meaning of Recommendation Degrees (U.S. Preventive Services Task Force, Ref [37]).

Degree of recommendation	Meaning
A	Extremely recommendable (good evidence that the measure is effective and benefits outweigh the harms)
B	Recommendable (at least, moderate evidence that the measure is effective and benefits exceed harms)
C	Neither recommendable nor inadvisable (at least moderate evidence that the measure is effective, but benefits are similar to harms and a general recommendation cannot be justified)
D	Inadvisable (at least moderate evidence that the measure is ineffective or that the harms exceed the benefits)
I	Insufficient, low quality or contradictory evidence; the balance between benefit and harms cannot be determined.

Table 5. Strength of Consensus.

Strength of consensus	Definition*
Strong	>80% consensus
Moderate	50–79% consensus
Weak	<50% consensus

*Quorum defined as 80% of participants available for vote.

evidence ranking, or consensus when evidence was lacking, followed by assigning consensus rankings. The consensus determination was performed during in-person meetings or via teleconference or written communications with a quorum of 80% of the contributing authors determining recommendation strength. Consensus rankings were outlined as strong, moderate, or weak based on agreement, as defined in Table 5.

This document provides recommendations regarding infection prevention, management and control. However, these recommendations should not be construed as a standard of care. Neurostimulation and infection management practices vary worldwide. It is important to address the conflicting nature of evidence and the need for consensus. Evidence and consensus are not mutually exclusive, which may be the perception at first glance. Rather, evidence assessment, regardless of the strength, requires interpretation for clinical application.

SUMMARY OF INFECTION PREVENTION AND MANAGEMENT MEASURES RECOMMENDED BY THE NACC

Table 6 presents the summary recommendations, evidence grade, and consensus strength for infection prevention and management measures recommended by the NACC. The remainder of this document discusses the evidence in greater detail.

SURGICAL SITE INFECTIONS

Neuromodulation and Surgical Site Infections

Although specific neuromodulation research on SSIs is limited, the evidence that exists provides some insight. In 2004, Follett et al. (38) reviewed data pertaining to infections associated with intrathecal drug delivery and SCS systems. They determined that these implantable device infections share similarities with SSIs associated with other implantable devices, including cardiac and neurosurgical devices (e.g., cerebrospinal fluid shunts). A majority of reported infections occurred at the generator site (54%), with lower infection rates at the SCS electrode implant site (17%) and lumbar incision (8%). *Staphylococcus* species were the most common causative agents, present in 48% of cases. In a retrospective review, Engle et al. (19) examined 131 patients who underwent treatment with implantable pain therapies (58% intrathecal drug delivery systems and 42% SCS systems) in high-risk populations (80% of the study population had a diagnosis of cancer) (Table 1). The overall reported infection rate was 2.8%, with all infections occurring at the site of the pulse generator or pump pocket. Extended surgical time was identified as a statistically significant risk factor for an SSI. In a randomized controlled trial (RCT) comparing SCS vs. conventional medical management (CMM), Kumar et al. (22) reported a 10% infection/wound breakdown complication rate (Table 1). Mekhail et al. (20) retrospectively evaluated 707 consecutive SCS cases, 527 of which went on to implant, and described an infection rate of 4.5%. In their retrospective review, 9% of all diabetic patients developed infections (Table 1). Recently, Hayek et al. (16) retrospectively reviewed 345 patients, 234 of whom received implants, and reported an infection rate of 4.3%. The median time from implant to the occurrence of infection was 1.99 months (95% CI 0.95–5.37; Table 1).

Criteria for Defining Surgical Site Infections

Superficial infections, deep infections involving the generator/pump and/or leads/catheters, and epidural abscesses are the three major types of infections associated with neuromodulation. The CDC has previously defined superficial and deep incisional SSIs (39). Superficial SSIs involve the skin and subcutaneous tissue surrounding the incision and are defined as infections occurring within 30 days after the operation. Deep incisional infections involve the deep soft tissue including muscle and fascia. When an implantable device is involved, the responsible time frame for deep infection is up to one year postoperatively. An incisional SSI that extends into the fascia and muscle layers is classified as a deep incisional SSI. Epidural abscesses have also occurred with both SCS trials and implants and are associated with significant medical risks that require immediate and attentive medical care (40,41).

Bacteria Associated With Surgical Site Infections

A majority of SSIs originate from bacterial contamination with the patient's own skin flora (42). Neuromodulation implantation techniques are considered clean surgical procedures. Organisms most responsible for SSIs for clean surgical procedures include *Staphylococcus aureus* and coagulase-negative staphylococci (e.g., *Staphylococcus epidermidis*), with *Escherichia coli*, and *Pseudomonas aeruginosa* being less common (43,44). Approximately two-thirds of implantable device infections are caused by *S. aureus* or coagulase-negative staphylococci (14). Unfortunately, *S. aureus* is becoming more resistant to clinically tried antibiotics, including newer

Table 6. The NACC Recommended Infection-Management Practices With Defined Origin of Practice.

Statements	Origin of recommended practice*	Evidence levels	Recommendation strength	Consensus strength
Preoperative practices				
Identify and treat all remote infections for neuromodulation trials and implants	CDC IA	II-2	B	Strong
Optimize glucose control for neuromodulation implants	CDC IB	II-2	B	Strong
Discontinue tobacco use for neuromodulation implants	CDC IB	II-2	B	Strong
Decolonize MSSA and MSRA carriers through the application of mupirocin nasal ointment and chlorohexidine baths		I	A	Strong
Utilize preoperative antibiotics for neuromodulation trials and implants	CDC IA and NICE	I	A	Strong
Utilize preoperative weight-based antibiotic dosing for neuromodulation trials and implants	CDC IA and NICE	I	A	Strong
Use appropriate preoperative timing (within 1 hour prior to surgical incision excluding vancomycin) of prophylactic antimicrobial administration for neuromodulation trials and implants	CDC IA, NICE, SCIP	I	A	Strong
Remove hair (when required) with electric clippers immediately before the surgical procedure	CDC IA and NICE	I	A	Strong
Perform preoperative surgical scrub for a minimum of 2–5 min with an appropriate antiseptic prior to neuromodulation trials and implants	CDC IB and NICE	II-2	B	Strong
Keep nails short and do not wear artificial nails for neuromodulation trials and implants	CDC IB and NICE	II-3	B	Strong
Do not wear hand or arm jewelry for neuromodulation trials or implants	CDC IB and NICE	III	B	Strong
Intraoperative practices				
Wear a surgical mask for neuromodulation trials and implants	CDC IB	II-3	B	Strong
Wear a cap or hood to fully cover hair for neuromodulation trials and implants	CDC IB	II-3	B	Strong
Use sterile gown and gloves for neuromodulation trials and implants	CDC IB	II-3	B	Strong
Double glove	CDC II and NICE	II-1	B	Strong
Utilize chlorhexidine gluconate for preoperative skin antiseptic agent	CDC IB and NICE	I	A	Strong
If an incise drape is used, then iodophor-impregnated drape for neuromodulation implants are recommended	NICE	I	A	Strong
Use laminar flow and HEPA filters in OR for neuromodulation implants	CDC IB	I	A	Strong
Limit procedure room traffic for neuromodulation trials and implants	CDC II and NICE	I	A	Strong
Keep procedure room doors closed during neuromodulation trials and implants	CDC IB	II-3	B	Strong
Limit tissue trauma, maintain hemostasis, eradicate dead space, and avoid electrocautery at tissue surface	CDC IB and NICE	III	B	Strong
Irrigate with saline through a bulb syringe prior to closure of surgical wound		I	B	Strong
Employ implant strategies to limit operative time		II-2	B	Strong
Postoperative practices				
Apply an occlusive dressing following neuromodulation trials and implants for 24–48 hours	CDC IB and NICE	II-2	B	Strong
Do not routinely use topical antimicrobial agents for surgical wounds that are healing by primary intention	NICE	I	B	Strong
Understand maximum time criterion for defining a deep surgical site infection of an implantable device (1 year postimplant)	CDC	III	B	Strong
Do not continue antibiotics into the postoperative period for neuromodulation trials and implants beyond 24 hours	SCIP	I	A	Strong
Educate patient and family on proper incision care, symptoms of SSI, and importance of reporting symptoms	CDC II and NICE	III	B	Strong
Wash hands before and after dressing changes	CDC IB	III	B	Strong
Use sterile technique for dressing changes	CDC II and NICE	III	B	Moderate
When SSI is suspected, prescribe an antibiotic that covers the likely causative organisms. Consider local resistance patterns and culture results in choosing an antibiotic	NICE	III	B	Strong

*The origin of recommended practice defines the supporting surgical guideline. CDC, centers for disease control; MRSA, methicillin-resistant *S. aureus*; MSSA, methicillin-sensitive *S. aureus*; NICE, National Institute for Health and Care Excellence; SCS, spinal cord stimulation; SCIP, surgical care improvement project; SSI, surgical site infection.

antibiotics. The number of cases of methicillin-resistant *S. aureus* (MRSA) is increasing (45). With implantable devices, infections can be challenging to treat, persistent, and often require the removal of the device secondary to the formation of biofilm around the implantable device (14). Reasons for lack of efficacy of antimicrobial agents in the presence of a biofilm include inhibition of antimicrobial activity and poor penetration of antibiotics. Once a surgical implant has been in situ for an extended period of time, hematogenous spread from an unrelated infection is a common seeding pathway that can result in an implantable device infection.

RISK REDUCTION FOR SURGICAL SITE INFECTIONS

Efforts to reduce SSIs should occur throughout the perioperative (preoperative, intraoperative, and postoperative) process. Implanting physicians need to know, understand, and put into practice the guideline recommendations from established organizations including the CDC, SCIP, and NICE (Table 6). Risk reduction strategies for each area of the perioperative process will be discussed here, with associated evidence grading and, when available, the associated recommending organization.

PREOPERATIVE WORKUP

The preoperative evaluation of the patient is an important process for several reasons. Patient education during this stage is highly valuable, but it also lends to the important identification of risks and discussions on risk reduction.

Medical History

Obtaining a comprehensive medical history and appropriate examination is important for insuring that a patient is an acceptable candidate for neuromodulation therapy. Certain diseases and medical comorbidities confer an intrinsically higher risk of infection. The risks, once identified, should be mitigated in the appropriate fashion and should be discussed with patients so that they can make informed decisions regarding progressing with implantable pain therapy surgery.

The history should focus on patients' previous surgical experiences and the occurrence of previous infections (perioperative or nonsurgical), excessive bleeding, or poor wound healing. A thorough medical history, including a broad assessment of organ system function, should include a review of neurologic, cardiovascular, pulmonary, renal, hepatic, hematologic, and endocrine systems. Optimization of health status should be discussed with the patient and medical care team before elective surgical implant.

Optimizing Medical Comorbidity Management

Certain comorbidities, including tobacco use, uncontrolled diabetes, malignancy, human immunodeficiency virus (HIV), untreated remote infections (e.g., urinary tract infections), preoperative steroid use, *S. aureus* carriers, and anticoagulation use may result in a greater risk of infection and can be potential relative contraindications to the implantation of neuromodulation devices until such conditions are well controlled or eliminated.

When the patient's history documents comorbid conditions, risk-mitigation strategies should commence (46). A retrospective case control analysis found diabetic patients to be 3.5 times as likely and obese patients to be 2.2 times as likely to experience infection after orthopedic spinal operations compared to nondiabetic and nonobese controls, respectively (47). Hyperglycemia has also been found to be an independent risk factor for SSI in patients without diabetes undergoing orthopedic trauma surgery, as well as in diabetic patients undergoing open heart surgery (48,49). Smoking has also been shown to be associated with elevated risk of SSI following spine operations, joint arthroplasty, and cardiac surgery (46,50–52). Abstaining from smoking for four weeks with transdermal nicotine patches has been found to lower incision infection rates among smokers to a level similar to that of nonsmokers (53). A review of 635,265 patients undergoing surgery found that chronic preoperative steroid use increases the risk of surgical infections by 1.7–3.4 times and increases the risk of mortality 3.92 times compared to patients not taking preoperative steroids (54). Caution is also advised in individuals on high-dose opioid therapy. Opioids modulate the immune system and can have inhibitory effects on the humoral and cellular immune response (55,56).

Chronic pain can be associated with anorexia, malnutrition, and gastrointestinal distress. In some cases, patients become malnourished to the point of increasing the risk of infection. It should be a goal to optimize nutrition prior to implant, if possible.

HIV may be a relative contraindication for SCS implantation due to increased risk of procedure-related infections. Most studies have found that HIV-positive patients are at elevated infection risk during surgical procedures, particularly patients with a high viral load (30,000 copies per mL or more) (57). However, postoperative mortality rates among HIV-positive patients receiving antiretroviral therapy tend to be relatively low, leading some researchers to argue that HIV itself should not be a contraindication to operative procedures (58).

Patients with malignancies who are currently undergoing chemotherapy may be at an elevated risk for infection and may be high-risk candidates for device implantation. Prior to undergoing a neuromodulation procedure, it is recommended that medical information be obtained on the white blood cell count and neutrophil count. In addition, an understanding of a patient's chemotherapeutic agents will also assist with perioperative planning. Chemotherapeutic agents, such as bevacizumab (humanized monoclonal antibody), have been associated with multiple wound healing complications (59). Preoperative planning and a discussion with the hematologist/oncologist will assist in determining optimal timing for implantation based on appropriate drug cessation and re-initiation times. If possible, it is recommended that irradiated areas be avoided for surgical implantation. Compromised wound healing is commonly seen in irradiated tissues (60). One study found that patients with cancer are at relatively low risk of infection following SCS implantation (3.4%), suggesting that cancer patients may not be at substantially elevated risk when not immunocompromised or undergoing chemotherapy (19).

Consensus Point 1. The NACC recommends the patient consult with the physician controlling diabetic management in an effort to optimize HbA1C and glucose control prior to neuromodulation procedures, if possible.

Consensus Point 2. The NACC recommends smoking cessation, if the patient will comply with this advice, for at least four weeks before neuromodulation procedures. If the patient will not stop smoking, transitioning to a transdermal nicotine patch under the oversight of the patient's primary care provider may be helpful. Abstaining from smoking for four weeks with transdermal nicotine patches has been found to lower incision infection rates among smokers to a level similar to that of nonsmokers (53).

Consensus Point 3. The NACC recommends limiting steroids in the immediate preoperative period, if possible. If the patient is receiving chronic steroid therapy, a discussion should occur with the prescribing physician to determine if appropriate management strategies can be taken to limit or reduce the steroid dose in the perioperative period.

Consensus Point 4. The NACC recommends consideration of treatment of potential infection sources before neuromodulation procedures, including (but not limited to) dental infections, skin, and urinary tract infections.

Consensus Point 5. The NACC recommends attempting to optimize nutritional status in the perioperative period for malnourished patients; however, there are no data to guide the optimal time frame or goals for optimization. Consultation with the patient's primary care physician and/or a nutritionist may be prudent.

Consensus Point 6. The NACC does not recommend that HIV be viewed as a contraindication and recommends that, if proceeding with implant, the patient may need to consult with the infectious disease specialist to optimize the viral load.

Consensus Point 7. The NACC recommends that patients with active malignancy, ongoing chemotherapy, or radiation consider consultation with their oncology specialist to aid in quantifying the level of risk of implantable device surgery vs. the benefit of the therapy.

Management of Anticoagulation Therapy

The presence of a hematoma can lead to wound dehiscence and serves as an excellent bacterial growth medium, which can eventually cause secondary infection. Therefore, bleeding risks also play a role in infection reduction. The NACC has made recommendations on reduction of bleeding risks in a companion article (61).

Certain patients have elevated perioperative bleeding risk due to bleeding disorders or current anticoagulation therapy. A history of easy bruising, previous bleeding surgical complications, and bleeding from the gums are important to detect before surgery. A thorough discussion of bleeding risks secondary to medication is important, and should include all prescription drugs and over-the-counter medications that may impact clotting or bleeding risks. A collaborative multisociety group (The American Society of Regional Anesthesia and Pain Medicine, the European Society of Regional Anaesthesia and Pain Therapy, the American Academy of Pain Medicine, the INS, the North American Neuromodulation Society, and the World Institute of Pain) and the NACC have completed best practice recommendations on proper methods of managing anticoagulation during the preoperative period (61,62).

Discontinuing anticoagulation therapy holds intrinsic risks and it is recommended that medication management strategies be discussed with the patient and the prescribing physician. The benefits of intervention must outweigh the risk of medical morbidity when discontinuing anticoagulant therapy. The final decision to withhold these medications should be determined by the prescribing physician, who should assess the risk for discontinuing anticoagulants and formulate the safest perioperative plan to discontinue medication or bridge it with short-acting anticoagulants. The placement of neurostimulation devices is elective and if no pathway exists to withhold the anticoagulant medication in a safe fashion, the procedure should not be performed.

Consensus Point 8. The NACC recommends appropriately managing anticoagulation therapy to manage bleeding risks effectively, based on published clinical anticoagulation guidelines. Shared decision-making should occur between the implanting physician, patient, and physician prescribing the anticoagulant therapy.

Physical Examination

The physician and care team should evaluate the patient for skin lesions, active infections, and local skin abnormalities at the site of implant. The physical examination should also evaluate for fragile skin secondary to chronic steroid use, aging, or concomitant disease. Abnormalities in vital signs should be noted and it is recommended that an appropriate investigation for the causative factor occur.

Consensus Point 9. The NACC recommends a careful examination of the skin in the area of implant before surgery. If local infection or skin abnormalities exist the intended procedure should be canceled or delayed until resolution.

Consensus Point 10. The NACC recommends attention to vital signs, such as temperature, heart rate, and blood pressure, as possible indications of systemic infection.

Laboratory Evaluation

Appropriate laboratory evaluation before neuromodulation device implantation has not been clearly defined. Specific laboratory tests may help identify risk factors for infection, bleeding, and organ failure. Studies have shown that many of these tests may be unnecessary, as they rarely yield abnormal results. Furthermore, among the small percentage of results that are abnormal, treatment is usually not affected (63,64). However, depending on patient history and physical findings, preoperative laboratory tests may be beneficial. For example, indicated preoperative testing for patients with cardiovascular disease includes hemoglobin, BUN, creatinine, and glucose. Patients with pulmonary disease should also have tests measuring hemoglobin and glucose (65). Additionally, other conditions that impair organ function may indicate appropriate laboratory blood testing, such as creatinine testing for kidney disease. Patients undergoing anticoagulation therapy should discontinue their anticoagulants after obtaining clearance and undergo appropriate preoperative testing on coagulation status when indicated.

Despite reservations about the use of laboratory blood testing in the absence of specific indications, certain laboratory values can indicate heightened risk for infection. For patients undergoing total hip arthroplasty, a white blood cell count greater than 11×10^9 per liter was indicative of infection risk (66). Similarly, patients with preoperative erythrocyte sedimentation rates (ESRs) of greater than 30 mm per hour were more likely to experience postoperative infections. A level of C-reactive protein (CRP) greater than 10 mg per liter was also indicative of infection, although not specific.

Preoperative Screening for MSSA and MSRA

The leading bacterial cause of SSIs is *S. aureus*, accounting for approximately 30% of all SSIs (67). In orthopedic and neurosurgical procedures, *S. aureus* is responsible for 50–60% of SSIs (68). Carriers of both methicillin-sensitive *S. aureus* (MSSA) and MRSA are epidemiologically linked to a higher risk (two to nine times higher) for an SSI (67,69,70). Carriers of bacteria often harbor the bacteria in multiple anatomical areas, including the anterior nares, perianal, and groin regions. Carriers may be classified as transient, intermittent, or persistent carriers. In individuals undergoing orthopedic implants, a high level of nasal carriage of *S. aureus* was the most important risk factor for developing an SSI (71). Greater than 80% of healthcare-associated *S. aureus* infections are endogenous (72–74). In addition, in individuals who develop an *S. aureus* SSI, the bacteria isolated

from the infected areas matches that of the nares 80–85% of the time (75). Approximately, 25–30% of the general population is colo-

Table 7. Prophylactic Antibiotic Recommendations.*

Antibiotic	Standard intravenous dosing	Timing prior to incision	Redosing interval	Indications
Cefazolin**	1 g ≤ 80 kg 2 g > 80 kg 3 g > 120 kg	Within 30–60 min	3–4 hours (CrCl > 50 mL/min) 8 hours (CrCl 20–50 mL/min) 16 hours (CrCl < 20 mL/min)	First-line
Clindamycin	600 mg ≤ 80 kg 900 mg > 80 kg 1200 mg > 120 kg	Within 30-60 min	6 hours (CrCl > 50 mL/min) 6 hours (CrCl 20-50 mL/min) 6 hours (CrCl < 20 mL/min)	β-lactam allergy
Vancomycin	1 g ≤ 80 kg 2 g > 80 kg 3 g > 120 kg	Within 120 min	8 hours (CrCl > 50 mL/min) 16 hours (CrCl 20-50 mL/min) None (CrCl < 20 mL/min)	β-lactam allergy Known MRSA colonization

*Modified from Bratzler et al. (89), Alexander et al. (90), and Bratzler et al. (91).
**In an effort to simplify cefazolin weight-based dosing, the American Society of Health-System Pharmacists (ASHP) recommends 2 g for individuals weighing <120 kg and 3 g for individuals weighing ≥120 kg. MRSA, methicillin-resistant *S. aureus*; CrCl, creatinine clearance.

reach and maintain MIC prior to incision and throughout surgery. Unfortunately, Medicare data have demonstrated that only 55.7% of patients receive prophylactic antibiotics within one hour before incision, as recommended for all antibiotics excluding vancomycin (93). Olsen et al. (47) in orthopedic spinal operations demonstrated that suboptimal timing of prophylactic antibiotic therapy was associated with a significant risk of SSI (odds ratio 3.4, 95% CI = 1.5, 7.9). Preoperative antibiotics should be administered intravenously prior to incision time (i.e., 30–60 minutes prior to incision for cephalosporins, sulfonamides, and aminoglycosides or within 120 min of incision for vancomycin).

The duration of action of an antibiotic is influenced by the agent's half-life and the patient's renal function, as the kidneys excrete the majority of antibiotics used in neuromodulation procedures. Clindamycin is the only antibiotic used for antimicrobial prophylaxis in neuromodulation procedures that is not affected by renal function. Based on the duration of neuromodulation surgical procedures, redosing is typically not needed (Table 7).

Consensus Point 14. The NACC concurs with the CDC, NICE, and SCIP recommendations for the preoperative use of antibiotics for neuromodulation procedures (see Tables 6 and 7).

Surgical Scrub

Duration of scrub and the antiseptic solution used are the two most important factors when defining an optimum surgical scrub. Commercially available antiseptic solutions in the United States contain alcohol, chlorhexidine, and/or povidone iodine. The duration of the surgical scrub appears to be the most important factor to ensure adequate hand hygiene and to limit bacterial counts. Surgical hand washing lasting between 2 and 5 min results in statistically fewer colony forming units on cultures compared to hand washing techniques of lesser duration (94–96). There are data to support the use of chlorhexidine over povidone iodine due to a reduction in hand bacterial counts (97,98).

Hand and arm jewelry should be removed prior to a surgical scrub as its presence has been associated with higher bacterial counts on the hands of healthcare workers even after hand washing (99). In addition, nails should be kept short and artificial nails should not be worn. Healthcare workers wearing artificial nails have higher bacterial counts under their nails after hand washing, and an outbreak of *Serratia marcescens* SSIs was linked to an OR nurse wearing artificial nails (100,101). Additionally, longer nails are thought to be associated with higher rates of glove perforation (5).

Consensus Point 15. The NACC recommends that physicians perform a preoperative surgical scrub for a minimum of 2–5 min with an appropriate antiseptic prior to neurostimulation trials and implants.

INTRAOPERATIVE RISK REDUCTION

Surgical Skin Preparations

A major source of pathogens for an SSI is the patient's skin. A fundamental component of the perioperative effort to reduce SSIs is the use of an appropriate skin antiseptic agent and preparation technique. Ideally, antiseptic agents should have the following characteristics: 1) broad-spectrum antimicrobial activity, 2) rapid bactericidal activity, 3) prolonged efficacy following application, 4) maintenance of bactericidal and bacteriostatic effects in the presence of organic matter, 5) limited systemic exposure, and 6) lack of skin irritant properties (102).

The two agents commonly utilized for skin preparation are povidone-iodine and chlorhexidine-based solutions. Both povidone-iodine and chlorhexidine-based products are often combined with isopropyl alcohol. Isopropyl alcohol is an effective bactericidal agent that disorganizes cell membrane lipids and denatures cellular proteins (102). Isopropyl alcohol has been shown to increase the antimicrobial activity of both products.

Povidone-iodine is an iodophor, a complex of iodine and organic carrier compounds (103). These complexes destroy microbial protein and DNA and are active against a wide spectrum of bacteria and

Table 8. Indications for Vancomycin Use.

1. Beta-lactam allergy
2. MRSA colonization
3. Patients with recent, prolonged hospitalization, or institutionalized (nursing home, long-term care facilities, etc.)
4. Surgical procedure is being performed in a facility with a recent outbreak of MRSA
5. Endemic presence of MRSA in the community

fungi. Specifically, povidone-iodine is a complex of bactericidal iodine with the polymer polyvinylpyrrolidone. In order for iodophors to have significant bactericidal activity, 2 min of contact is required to release free iodine, which is responsible for the antimicrobial activity. *In vitro* data have demonstrated significant residual bacterial counts when exposure time is limited. Iodophors' antimicrobial effects may be inhibited or neutralized by organic compounds (e.g., blood). Adverse reactions to povidone-iodine include contact dermatitis and impaired wound healing secondary to its cytotoxic effects on fibroblasts and keratinocytes (the predominant cell type in the epidermis).

The role of chlorhexidine-based products is expanding for the prevention of SSIs (104). Chlorhexidine gluconate is active against a broad spectrum of gram-positive and gram-negative bacteria, yeasts, and molds. Its mechanism of action includes the disruption of cytoplasmic membranes. Chlorhexidine-based products are superior to iodophors secondary to their residual antimicrobial effects, rapid activity, high binding to the skin, and lack of negative inhibitory effects by organic compounds. In addition, specific strains of *S. aureus* have been shown to be resistant to the antimicrobial effects of povidone-iodine. Both skin irritation and erythema have been documented with chlorhexidine-based products.

In clinical studies, chlorhexidine-based products have been shown to be superior to povidone-iodine based products in both reducing skin surface flora at the incision site (surrogate study) and reducing SSIs. In foot, ankle, and shoulder orthopedic models, chlorhexidine-based products were associated with lower levels of skin bacterial counts (105,106). Darouiche et al. (107) examined the rates of SSIs in patients who underwent surgery in six hospitals and were either assigned to chlorhexidine-alcohol or povidone-iodine skin preparation. The overall rate of SSIs was significantly lower in the chlorhexidine-alcohol group than the povidone-iodine group, 9.5% vs. 16.1%, respectively. In a systematic review, meta-analysis and cost analysis comparing chlorhexidine with iodine for preoperative skin antisepsis with respect to preventing SSIs and costs, chlorhexidine was found to be more clinically and cost effective in preventing infections (108). In the meta-analysis portion, nine RCTs with a total of 3614 patients were analyzed.

From a safety standpoint, the U.S. Food and Drug Administration (FDA) have not approved chlorhexidine for use before neuraxial procedures because of the absence of clinical safety evidence. However, a large retrospective cohort study examining 11,095 patients who received a total of 12,465 spinal anesthetics demonstrated no increased risk of neurological complications attributed to a spinal anesthetic when chlorhexidine was used (109). If a skin antiseptic agent containing alcohol is utilized, the agent must be allowed to dry before draping, so as to reduce the likelihood of a surgical fire occurring during electrocautery. In conclusion, chlorhexidine-based products for surgical skin preparation appear to be the agents of choice for neuromodulation procedures. Chlorhexidine-based products have a superior antimicrobial profile compared to iodophor solutions, and have been shown to reduce skin bacterial levels and SSI rates. Recent research has suggested that skin preparation with a combination of chlorhexidine and povidone-iodine may be superior to either agent alone (110).

Consensus Point 16. The NACC recommends the use of chlorhexidine-based products combined with isopropyl alcohol for skin preparation prior to neuromodulation procedures.

Surgical Attire

Maximal sterile barrier precautions (surgical cap, mask, and sterile gloves and gowns) for surgical procedures are recommended by the CDC, NICE, and SCIP. Surgical masks reduce the spread of nasopharyngeal bacterial contamination. Specifically, in 2004, the CDC and Healthcare Infection Control Practices Advisory Committee released a statement recommending the use of face masks for neuraxial procedures after an outbreak of bacterial meningitis following neuraxial procedures was linked to practitioners not wearing face masks (111). Changing of masks should be considered between cases, as the efficacy of this barrier has been shown to decrease significantly after only 15 min (112). Postsurgical infection outbreaks have also been traced to bacteria on the scalps of operating room personnel (113,114).

While there are no studies directly comparing the risk of SSIs with single vs. double gloving techniques, double gloving has clearly been shown in multiple studies to reduce the number of inner glove perforations (115). Therefore, double gloving should be highly considered for implantable device surgeries to both reduce the risk of SSIs as well as to protect the practitioner. Surgical glove exchange during certain stages of an operation has been shown to reduce glove contamination rates (115,116). Therefore, changing the outer gloves before handling and implanting the generator may reduce the risk of contamination (117).

Consensus Point 17. The NACC recommends maximal sterile barrier precautions as well as double gloving for implantation of implantable pain devices.

Operating Room Environment and Equipment

The operating room environment can also serve as a vector for pathogens if proper measures are not taken. Positive pressure ventilation should be maintained within the operating room to prevent the flow of air from the outside in. A multicenter RCT performed in 1982 by Lidwell and colleagues showed that joint arthroplasties performed in laminar flow, positive pressure operating rooms compared to conventionally ventilated operating rooms resulted in a reduction in airborne and patient wound bacterial contamination (118–122). In addition, the incidence of deep joint sepsis was reduced by 50%. Other studies have also shown that laminar-flow operating rooms and high-efficiency particulate air (HEPA) filters reduce SSIs and wound contamination compared to conventional airflow systems in spinal fusion and hip arthroplasty operations (123,124).

Operating room personnel are a major source of contamination in the operating room (125). The number of personnel, as well as traffic flow rates in the operating room, positively correlate with the degree of airborne contamination (126). Education, preoperative planning, communication, and limiting surgical time are the most effective measures to decrease traffic flow.

There are many potential sources of contamination from equipment within the OR (i.e., light handles, fluoroscopic C-arm, ultrasound probe). Contamination of sterile light handles has been reported to be as high as 14.5%; therefore, handling of operating room lights should be minimized (125,127). Biswas et al. evaluated the sterility of 25 C-arm drapes placed with aseptic technique after their use during spine surgery (128). All locations were contaminated at the end of the surgical case. The front, top half and the superior end of the image intensifier were associated with higher contamination rates. Therefore, all operating room personnel should avoid contact with the C-arm.

Consensus Point 18. The NACC recommends minimizing traffic flow through the operating room, use of sterile C-arm drapes, and

minimizing contact with overhead light handles and the C-arm drape.

Incise Drapes

Traditional cloth drapes are not recommended for implantable device surgery and have been shown to allow for increased bacterial penetration when wet (5,129). Plastic adhesive drapes that are not iodophor-impregnated may slightly increase the risk of SSIs; this may be due to their impermeable nature, which allows moisture to collect under the drapes and serve as a medium for bacterial growth (130). Iodophor-impregnated drapes may reduce the number of positive postprocedural skin cultures (131–133). However, there are no data to support their routine use for the reduction of SSIs (42,134). There are two studies comparing the rates of SSIs for iodophor-impregnated drapes vs. no drapes and neither showed a significant difference (135,136). While the use of iodophor-impregnated drapes may be considered for high-risk patients, universal usage is not supported by the literature.

Consensus Point 19. The NACC recommends following the NICE recommendations that if adhesive drapes are used, iodophor-impregnated drapes should be used.

Surgical Training to Limit Infections

Potential implanters should have undergone formal training in a high-volume center with appropriate credentialing. The NACC recommends that implanters perform a minimum of ten cases as the primary implanter and under supervision. Training must encompass each facet of the operation, including patient selection, anatomy of the implant area, surgical technique, complication identification and management, and collaboration with colleagues (34).

Special comment is required for recommendations about medical and surgical education. The NACC serves an international community, with recommendations regularly refreshed. There is no uniform training program or credentialing standard that serves such a diverse international group. However, certain standards are required for safe implementation of neuromodulation. First, each implanter must be a physician with appropriate surgical training. Exclusive of physicians in active training programs, formal education (formal medical training within the country of practice) should be completed in the area of medicine or surgery, with appropriate formal and proctored cases of tissue management, with a focus on implantable technologies. For the neurosurgical community, this requirement is more apparent compared to the anesthesia/pain management community. In the United States, since formal programs exist for pain medicine and surgery, which are certified by the American Board of Medical Specialties and the American Council of Graduate Medical Education (ACGME), the NACC recommends that American implanters should have undergone and completed such training. This recommendation, however, does not devalue "legacy" or "grandfathered" practitioners who began using neuromodulation when such formalized graduate medical training was not available.

ACGME programs in the United States are not without challenge. Recent surveys suggest a lack of neurostimulation exposure (137), well under the ten cases recommended for primary implanters, and neurostimulation is not a requirement for completion of the fellowship. Thus, variability of existing trainees' skill sets will continue. In the future, formal society training and certification programs may further assist in meeting this education need.

The duration of surgery also influences postoperative infection risk, with longer procedure times being associated with higher infection rates (19,138).

Consensus Point 20. The NACC recommends that those who are credentialed for neuromodulation procedures perform a minimum of ten cases as the primary implanter and under supervision during training.

Consensus Point 21. The NACC recommends for physicians actively employing neuromodulation therapies, appropriate and complete medical training in surgery or medicine, with a focus on implantable technologies. The country of active practice must recognize this training, with appropriate credentialing within the country of practice. Furthermore, the NACC recommends that for those who do not receive training during an ACGME training program, proper hands-on continuing medical education be obtained and that the first ten cases in practice be overseen by a physician with previous credentialing at a Joint Commission-approved facility.

Influence of Trial and Implant Pathway

Multiple pathways exist for the trialing and implanting of neuromodulation devices. The two most common pathways consist of either a separate trial followed by separate full implant, or a staged trial and completion implant. A recent survey demonstrated that 98.6% of the respondents from the United States use a separate trial and separate implant pathway (15). Of the European respondents, 61.4% use a separate implant pathway with 38.6% using a staged trial and completion implant pathway. Concern has been raised about the possible infection rates associated with the staged trial and completion implant pathway. The current literature often does not discriminate between the technique of SCS for test period and implantation when it comes to reporting infection rates. Indeed, the literature poorly discriminates between infections following a trial period or infections following complete implantation. Recent research has examined infection rates for the staged trial and completion implant pathway under certain infection-control protocols.

May et al. have published consecutive patient series that for more than 22 years have tracked the incidence of trial and implant infections (139–141). During these series the authors were able to improve infection rates with staged trials and completion implants. May et al. (139) reported on the first 59 SCS patients (1993–1997) having a test period, and 11 (18.6%) had an infection and required trial lead, anchor and extension removal. Improvements in standard operating procedures (1997–2000), including more secure exit-site dressing of extensions, reduced the infection rate to 7.5% (3/40). All infections were superficial and did not result in epidural abscess. However, two of 81 implanted patients had their devices explanted due to infection (2.5%).

Following further protocol changes (introduction of hydrocolloid exit-site dressing), Rudiger et al. (140) reported on the second consecutive series of 84 patients; 68/84 progressed to a completion implant. During the 84 trials only 1/84 devices required removal due to infection (1%). However, 3/68 completion implants showed signs of infection (4.4%), but all were treated with antibiotics and none required device explantation. At this time, there were two implanting physicians, one with 16 years experience and the other with 7 years experience. The more experienced implanter had only 1/61 infections (1.6%—trial period only) and the less experienced had 3/23 infections (13%—following completion implant, not requiring explantation).

Following still further changes (preoperative skin cleansing regimen and exacting compliance with antibiotic prophylaxis), the third consecutive series of SCS patients was reviewed by Thomson et al. and results presented at several conferences (141). Of 171 patients with 164 full implantations, 38 of 164 had a single-stage full implant

as they were pre-existing SCS patients, 31 of 38 patients had an SCS system upgrade replacement, and 7 of 38 were part of the simultaneous refractory angina study where protocol was to implant the SCS after an on-table trial; 126 of 133 (95%) patients had a successful test period and progressed to full implantation. There was one (of 133) trial period infection (0.75%) but 3 of 126 completion implant patients (2.4%) had an infection, of which 2 of 126 were explanted (1.6%). Of interest, only 1 of 38 single-stage full implants (2.6%) had infection and was explanted.

Techniques used to reduce infection in staged and extended-trial periods included preoperative patient skin cleansing, MRSA screening and appropriate decolonization, surgical technique, exit-site dressing management with hydrocolloid and nontouch strapping, and compliance with the perioperative antibiotic regimen. If these measures are taken, the subsequent infection rate requiring explantation of full implant (1.6%) is little different from that seen after single-stage full implant (2.6%) or in the literature (3.4% [13] or 5% [142]). Based on the current literature, under appropriate infection-control conditions, the staged trial and completion implant pathway can be utilized in select patients without a significant increase in infection rates.

Consensus Point 22. The NACC recommends taking appropriate measures to limit infections in staged and extended trials, including the use of occlusive dressings.

Surgical Techniques to Limit Infection

Tissue Management

Wound class has been previously demonstrated to have an approximately linear relationship with subsequent SSI development, with Class I/clean surgical wounds being associated with the lowest risk of SSIs (143). Increased wound size also correlates with increased rates of SSIs (144), with a greater area of devitalized tissue providing an isolated and protective niche for bacterial inoculum to grow unimpeded from host defenses. Desiccation of the wound edges, in addition to peripheral vasoconstriction and poor tissue perfusion secondary to hypothermia and hypovolemia, allow for increased bacterial accumulation within the wound (145). Thus, tissue necrosis, foreign bodies, seromas, hematomas, and poor tissue perfusion can result in increased SSI rates.

Incisions should be executed with a scalpel with a clean cut, and the incision site made as small as possible for both leads and battery site. Minimizing dead space in the battery pocket also limits seroma and hematoma development. Epinephrine used in conjunction with a local anesthetic has been suggested to increase both risk of delayed healing due to vasoconstriction at the incision site as well as increased bacterial count. High epinephrine dose has been suggested to inhibit skin fibroblast migration, while lidocaine prevents initial wound signaling and mast cell degranulation via nociceptive blockade (144). Cautious use of epinephrine should be implemented in order to minimize tissue damage and decrease postoperative infection rate. However, this risk must also be weighed against the potential benefits of reduced bleeding due to vasoconstriction, as blood can serve as a medium for bacterial growth.

Consensus Point 23. The NACC recommends appropriate intraoperative tissue management and limiting surgical tissue trauma.

Electrocautery

There is no strong evidence showing that electrocautery directly affects SSI rates. However, studies have shown that electrocautery is associated with decreased intraoperative blood loss, incision time, and postoperative pain (146,147). Electrocautery has been shown to significantly decrease the threshold for bacterial contamination compared to electric cutting current and even more so compared to cold knife (148). Compared to scalpel and ultrasonic desiccator, patients operated on with electrocautery had significantly higher proinflammatory cytokines in their wound drains (149). Care must be taken to avoid excessive electrocauterization, which can lead to thermal tissue damage, and has been found to decrease antibiotic penetration and hinder macrophage and neutrophil migration to the wound, resulting in delayed removal of necrotic tissue and bacteria (144). A prospective RCT (150) demonstrated that monopolar electrocautery was associated with inferior wound healing compared to a tissue sealing-cutting device in terms of SSI, wound dehiscence, and unhealed wound rate. Intraoperative bleeding should therefore be controlled primarily with only light electrocautery (144,148). While excessive electrocautery use at the tissue surface should be avoided, it may be beneficial to maximize hemostasis and reduce surgery time, which have both been shown to be associated with decreased SSI rates (1).

Wound Irrigation

Currently, no official practice guidelines or recommendations specifically define best practices for surgical wound irrigation (151). Three major irrigation variables (delivery method, volume, and solution additives) need to be evaluated. Traditionally, wound irrigation is performed to remove bacteria and debris that have contaminated the wound during the surgical procedure. Delivery method is based on pressure (high-pressure is 15–35 psi and low pressure is 1–15 psi). For clean operative wounds, irrigation with a bulb syringe is recommended. Higher pressures can result in deep bacterial seeding in tissues (151). Currently, no official irrigation volume recommendations exist; however, animal studies have suggested that larger volumes are more effective (152). Often surgical irrigation is enhanced with additives including antibiotics, surfactants, and antiseptics. Based on limited clinical data, the addition of antibiotics to the irrigation fluid has not been shown to be superior to using saline alone (88,152–155). Also, the addition of antibiotics to the irrigation solution raises concern for development of antibiotic resistance and the potential for tissue toxicity (88,155). Both benzalkonium chloride and bacitracin have been associated with impaired wound healing (153,156).

Consensus Point 24. The NACC recommends surgical irrigation with saline through a bulb syringe before closure of the surgical wound.

Dead Space and Skin Closure

Wounds should be closed using a layered technique. Simple interrupted sutures are recommended for deep layers as such sutures limit the risk of wound edema or tissue strangulation, are stronger under tension, and reduce the affected wound area in the event of bacterial seeding. Running locked sutures should be avoided unless required for additional hemostasis, given the associated risk for impaired tissue microcirculation (144). A running subcuticular suture or staples can be used for skin closure. Care should be taken to avoid tissue strangulation. A clinical study comparing closure of midline abdominal incisions with small stitches placed 5–8 mm from the wound edge and <5 mm apart, vs. larger bites placed >1 cm from the wound edge, found that SSI was less common with smaller stitches (157). Surgical knot size should be small and made with minimal tension (144).

Suture options available to the surgeon include polyglactin 910 (vicryl), poliglecaprone 25 (monocryl), and nylon, all of which have

Table 9. Meta-Analyses and Systematic Reviews of Local Vancomycin Powder.

Authors	No. of studies	Total no. of patients in studies	Odds ratio for protection against surgical site infection
Chiang et al. (169)	10	5888	0.19 (95% confidence interval) 0.09–0.38
Bakhsheshian et al. (171)	15	Not reported	0.43 (95% confidence interval) 0.22–0.82 p value = 0.14
Khan et al. (172)	10	2574	Relative risk 0.34 (95% confidence interval) 0.17–0.66 p value = 0.02
Xiong et al. (170)	8	4592	0.22 (95% confidence interval) 0.07–0.63

different associated properties, absorption rate, and potential for tissue reaction (144). The decision of suture choice is largely surgeon-dependent and based on the area being closed (deep, subcutaneous, or subcuticular). Efforts should be made for the approximation of wound closure under minimal tension. There is conflicting evidence on whether or not staples increase the risk of SSI compared to sutures (157). A meta-analysis of RCTs in obstetric/gynecology, general, head/neck, and vascular operations suggested that staples were associated with significantly fewer SSIs compared to suture closure (158). A Cochrane review concluded that there was insufficient evidence to suggest a difference in SSI rates when comparing suture vs. staple closures for leg wounds after vein graft harvesting during cardiopulmonary bypass surgery (159).

Consensus Point 25. The NACC recommends closure of dead space with appropriate tension. Skin closure with either staples or suture should be at the discretion of the surgeon.

Topical and Envelop Antibiotics

There is insufficient evidence to support the use of topical antimicrobials for surgical incisions that are clean wounds healing by primary intention. An RCT by Kamath and colleagues showed no significant difference in the rate of SSIs when using or not using chloramphenicol ointment applied to the surgical incisions following operations for femur fractures (160).

Antimicrobial Patches. The first report on the use of a chlorhexidine-impregnated urethane sponge for epidural catheters placed for pain management was published in 1990 (161). In this RCT of 57 patients, microbial colonization of the catheter developed in 29% (9 of 31) of controls and 3.8% (1 of 26) of catheters that were managed with the chlorhexidine dressing ($p < 0.05$). No adverse events occurred with use of the dressing.

Interestingly, despite validation of this approach in one RCT, 11 years passed before a second confirmatory high-quality clinical trial was completed and the results published (162). This was a prospective randomized study of 55 women undergoing elective gynecological surgery followed by postoperative epidural analgesia. Positive cultures were found in 40.1% (11 of 27) of the control group compared with 3.4% (1 of 29) of the chlorhexidine Biopatch group (Biopatch; Johnson & Johnson Wound Management, Ethicon, Somerville, NJ, USA). A meta-analysis was later published in 2006 (163). The mean duration of the epidural catheter in situ was 3.5–3.7 days. Chlorhexidine-impregnated dressings reduced the risk of epidural catheter exit-site bacterial colonization to 3.6% (odds ratio 0.07, 95% CI, 0.02–0.31, $p = 0.0005$).

These results suggest that a chlorhexidine-impregnated dressing may be helpful in reducing the risk of exit-site colonization in high-risk patients undergoing percutaneous trials of neuromodulation therapy, such as SCS and PNS. A reduction in exit-site colonization may lead to a reduction in SSIs.

Consensus Point 26. The NACC does not recommend the routine use of chlorhexidine-impregnated dressings for neuromodulation trials. In high-risk patients with significant medical comorbidities, chlorhexidine-impregnated dressings may help reduce the risk of exit-site colonization and subsequent infection during trials.

Vancomycin Powder. Although not currently approved by the FDA, application of vancomycin powder to the surgical wound bed is one potential strategy that has been employed to mitigate the risk of deep SSIs. Vancomycin is a glycopeptide antibiotic that blocks polymerization of the bacterial cell wall (164). It is effective only for gram-positive bacteria, the most common microbes identified in infection of neuromodulation devices (165,166). No current guidelines or standard dosage recommendations are available for the use of intrasite vancomycin powder for the prevention of SSIs. The first use of topical vancomycin was reported in 1989—a prospective study of application of topical vancomycin to sternal wound edge after open heart operations (167). Sternal-infection rates dropped from 3.6 to 0.45% with the use of intrasite vancomycin powder ($p = 0.02$). Multivariate analysis showed that vancomycin and shorter operative times independently predicted reduced infection rates. In addition, animal studies have also suggested a protective effect for vancomycin powder. In a study of 20 New Zealand white rabbits that underwent lumbar partial laminectomy and wire implantation, the surgical sites were inoculated before closure by injecting *S. aureus* into the wound (168). Preoperative cefazolin was administered to all rabbits and vancomycin powder was placed in the wound of ten rabbits before closure. On day 4, the animals were sacrificed and bacteriological assessment occurred. The bacterial cultures were negative for all ten vancomycin-treated rabbits and positive for all ten control rabbits.

When examining the use of intrasite vancomycin powder for spine surgery, multiple meta-analyses and systematic reviews have suggested a protective effect in preventing SSIs, especially when surgical hardware is placed (169–173). The findings are summarized in Table 9. In one meta-analysis the number needed to treat to prevent one SSI was 36 patients (172). The literature sources used for

the systematic reviews and meta-analyses mainly consisted of retrospective cohort studies. In the one RCT included, the local application of vancomycin powder did not significantly reduce the incidence of infection in patients with surgically treated spinal pathologies (172,173). The complications associated with intrawound vancomycin are low. A recent systematic review documented an overall adverse event rate of 0.3% (174,175). Reported side effects included nephropathy, ototoxicity, supratherapeutic doses from systemic absorption, and seroma formation.

There is limited evidence supporting the use of vancomycin powder specifically for neuromodulation (174,176). Amrani et al. in a prospective case-control study examined the use of intrasite vancomycin powder and suggested that SSI rates may be decreased. Specifically, intraoperative powdered vancomycin's efficacy with SCS was investigated in 32 patients requiring a laminectomy for paddle implant and compared to 77 patients who did not receive vancomycin powder (176). The infection rate in the vancomycin group was 0%, while the infection rate in the group that did not receive vancomycin was 2.6%. Ghobrial et al. (175), in a retrospective review examining the use of intraoperative vancomycin powder during baclofen pump implants, suggested no improvements in SSI rates.

Before recommending vancomycin powder for neuromodulation procedures, high-quality studies examining efficacy and safety with large sample sizes and standardized dosing protocols are required.

Consensus Point 27. The NACC recommends additional studies prior to supporting the routine use of vancomycin powder for implantable pain therapies.

Antimicrobial Envelopes. In 2008, the FDA approved a bioabsorbable, polypropylene mesh antimicrobial envelope that releases minocycline and rifampin (TYRX^{TM}, Medtronic, Dublin, Ireland) for use in implantable cardioverter-defibrillator (ICD) implants, and in 2013 it gained approval for use in neuromodulation implants. TYRX has been shown to reduce ICD infection rates by 60% when used empirically, and by more than 87% when used selectively in patients considered at high risk for SSI (177–179). There are currently no specific data to support its routine use in SCS implants; however, considering the high level of evidence available for its ability to significantly reduce ICD implant infection, its use could be considered for patients considered at high risk for SSI undergoing SCS implant.

Consensus Point 28. The NACC recommends considering the utilization of antimicrobial envelopes around implantable pulse generators (IPGs) in patients at high risk of infection. Further studies examining efficacy in neuromodulation are warranted.

POSTOPERATIVE RISK REDUCTION

Postoperative Dressings

Early studies suggested that occlusive dressings augment wound healing and decrease the rate of SSI (180,181). However, more recent meta-analyses suggest that there is no difference in SSI rates when comparing occlusive dressings, advanced wound dressings (i.e., hydrocolloid, soft polymer), antimicrobial dressings, or leaving wounds uncovered (182,183). The CDC and NICE recommend the use of sterile occlusive dressings for 24–48 hours for incisions closed by primary intention (Category IB) (5). There are no data to support the use of occlusive dressings beyond 24 hours.

Consensus Point 29. The NACC agrees with CDC and NICE recommendations of using sterile occlusive dressings for 24–48 hours.

Postoperative Antibiotics

Prolonged antibiotic use in the postoperative period in cardiac, orthopedic, and plastic surgery has not been shown to improve outcomes (184). In spine surgery specifically, the administration of intravenous antibiotics beyond 48 hours increased the hospital stay and resulted in delayed normalization of body temperature and CRP levels (185). The SCIP recommends the discontinuation of antibiotics within 24 hours after surgery (7,8). Medicare data have demonstrated that in only 40.7% of patients was antimicrobial prophylaxis discontinued within 24 hours of surgery (93).

Consensus Point 30. The NACC recommends considering discontinuation of antibiotics within 24 hours following SCS implants. For high-risk patients, postoperative antibiotics should be considered.

Postoperative Wound Surveillance and Care and Patient Education

During the postoperative period, optimization of medical comorbidities should continue. Patients should be seen within 10–14 days of surgery to evaluate for appropriate wound healing and signs of SSI (186). Any evidence of a developing SSI requires closer follow-up. Sterile technique should be used for dressing changes. It is recommended that in routine cases, nonabsorbable sutures or staples be removed within 10–14 days based on the individual degree of wound healing (187). Patients and family members should be educated on signs and symptoms of an emerging SSI, incision care, and the importance of reporting any signs of infection, as early recognition of SSIs is the most important step in treatment.

Consensus Point 31. The NACC recommends appropriately educating the family and patient on signs and symptoms of SSIs.

Infection Identification and Management

Biologic complications most commonly present within three months of device placement (16); however, deep SSIs are defined by the CDC as occurring anytime within the first 12 months postimplant (5). Deep infections have been reported less frequently than superficial infections (188). Vigilence and recognition of an infection are the most important steps in management of an SSI.

Following implantation surgeries, white blood cell counts, ESR and CRP all rise transiently in the postoperative period, due to the body's stress response to surgery. Systemic diseases, such as malignancy and rheumatologic disorders, can affect baseline ESR and CRP levels. CRP levels rise 4–6 hours after acute tissue injury, peaking around the second or third postoperative day following total joint arthroplasty and spine surgery (189,190). ESR levels rise more slowly, peaking around the fourth or fifth postoperative day. CRP also returns to normal more rapidly (14–21 days) and predictably compared to ESR (190,191). Postoperative CRP kinetics are more responsive to and predictive of infection. Therefore, failure for CRP levels to normalize or an unexpected rise in CRP is a highly sensitive predictor of an SSI. Likewise, a normal CRP is highly sensitive for absence of an SSI.

Physical exam findings are also important in recognition of an SSI. Hyper- or hypothermia, tachycardia, hypotension, chills, erythema, or warmth overlying the surgical site, pruritis, purulent discharge, wound dehiscence, and swelling are all concerns for an underlying infection. Once an infection is suspected, treatment should begin immediately. Microbial culture is important to aid in correct antibiotic choice, although empiric initiation of antibiotics should not be delayed in a deteriorating patient, with planned refinement of treatment based on culture and sensitivity results when they become

available. Depending on the nature of the superficial infection, and the clinical picture, it has been recommended previously to consider conservative treatment (187). Superficial infection surrounding the IPG, remote to the neuraxial entry location, may be treated with an oral course of antibiotics and close follow-up (187,192). Superficial infections can track along the device to become more problematic infections. Imaging may be helpful in the identification of deep infections.

Except for superficial infections, which in some cases may be managed with appropriate wound care and antibiotics, infections often require the removal of the implanted devices. Formation of biofilm makes eradication of an infection involving any hardware very difficult. Relapse of infection reportedly occurs in over half of patients with ICDs left in place when generator pocket infections were identified (193). Similarly, conservative management of deep brain stimulator infections is successful in less than 40% of cases (194). When a deep SSI has been identified, explantation of implanted devices should be highly considered and recommended in the majority of cases.

Epidural abscess occurs spontaneously with an incidence of 2 per 10,000 hospital admissions (195), while incidence for implantable devices is unknown. Early diagnosis is crucial and progressive clinical phases of infection have been described by Van Zundert (195). Phase I presents as backache and local tenderness; phase II is associated with radicular pain and fever, with neck stiffness and rigidity occurring 48–72 hours later; phase III presents with motor, sensory or reflex depression (3–4 days later); and phase IV is paralysis. Neuraxial imaging can be used to detect the presence of fluid within or surrounding the epidural and adjacent tissue, and 80–90% of epidural abscesses are diagnosed with imaging. MRI with gadolinium contrast may be helpful. As of now not all neurostimulation therapies have MRI conditional labeling for the neuraxis. Prior to imaging, MR compatability should be verified. If imaging is required before device removal, the type of imaging modality (CT or MRI) needs to be considered.

If involvement of neuraxial structures is suspected, consultation with an infectious disease specialist (or medical microbiologist) is recommended. Mortality from an epidural abscess has been reported to range from 10 to 23%. Once neurologic deterioration has begun, emergent surgical decompression is necessary. Neurologic recovery is unlikely once paralysis has been present for >12 hours. In addition, once motor deficits have been present for >36 hours, full recovery is unlikely (196,197).

Staphylococcus spp. and *Enterococcus* spp. are commonly implicated, in decreasing order of frequency (5,198). Deep infections occur less frequently, with epidural abscess commonly caused by *S. aureus,* although gram-negative bacteria, mycobacteria, anaerobic bacteria, and fungi have been reported in the literature (199,200). Weight-based antibiotic regimens, including administration for an appropriate length of time, are crucial for the treatment of these complications. Speciation and culture sensitivities to guide antibiotic management and treatment are imperative. First-generation cephalosporins are commonly used to cover gram-positive bacteria. Fourth-generation cephalosporins broaden coverage to gram-negative bacteria, while cephalosporins do not cover enterococci (198). These trends are changing with the emergence of MRSA in the community. New drugs are available, including dalbavancin, oritavancin, and tedizolid (201).

When the decision for device removal and surgical debridement is made, the urgency of action is based on clinical presentation. Mindful planning allows for minimizing spread and containing the infection. After infected tissue is removed and purulent material drained, copious low-pressure irrigation is recommended to clear infected material. Surgical intervention does not obviate the need for appropriate antibiotics (13). The decision to close primarily, or to allow for secondary intention with serial packing or drain placement, is based on physician clinical decision-making (202). There are multiple reports of negative pressure wound therapy that seem to show promise (203,204). If questions remain regarding surgical approach, consultation with a general surgeon should be considered.

The time course of infection treatment is contingent on the degree and depth of the infection, the organism identified, and the health status of the patient. Collaboration with a wound care and infectious disease specialist is recommended to promote prompt treatment and recovery.

Consensus Point 32. The NACC highlights the importance of prompt recognition of SSIs and implementation of appropriate management strategies.

Consensus Point 33. The NACC recommends consultation with an infectious disease specialist to refine initial treatment, and to determine re-implant timing and risk-mitigating strategies if appropriate.

Consensus Point 34. The NACC recommends neuraxial imaging if clinical suspicion is high for a deep infection including epidural involvement is suspected.

Re-Implantation

Significant infection of a neuromodulation device requires explant. After the infection is resolved and risks of reinfection mitigated, re-implantation may be considered (205–208). Consultation with an infectious disease specialist (or medical microbiologist) prior to re-implantation is recommended. No formal data have described re-infection rates following re-implantation. Implantable pulse generator location change, timing of surgery, and preoperative preparation practices are largely anecdotal, with physician practice highly variable (15). Therefore, recommendations from the NACC are limited to considering re-implantation.

Consensus Point 35. The NACC recommends consideration of re-implantation after treatment for infection.

CONCLUSION

SSIs with implantable neuromodulation therapies are associated with significant morbidity, clinical consequences, and economic costs. Physicians performing implantable neurostimulation therapy procedures need to understand and consider appropriate infection prevention and management guidelines. When infections occur, prompt recognition and appropriate treatment are required. Further research is warranted, specifically for neuromodulation procedures, to continue refining guidelines and recommendations.

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Dr. Deer served as primary author, project organizer and editor; Drs. Deer, Provenzano, Hanes, and Pope performed literature searches and prepared evidence tables; Drs. Simpson, Krames, and Mekhail served as senior editors; all authors acquired or interpreted data, wrote sections of the manuscript, and provided critical reviews and editing.

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COMMENTS

These recommendations are an essential tool for physicians. It is a comprehensive guide providing useful suggestions for the daily prevention of infections and their management. The authors have provided an impressive job both in the analysis of a huge bibliography as in the quality of the synthesis.

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This extremely important work is vital and required reading for every person involved in the trialing and implantation of neuromodulation devices. It will deeply serve not only the implanting physician, but also the nurses, physician extenders, industry representatives and even the patients and families to the extent they can understand the points surrounding infection prophylaxis. Adherence to its tenants will further diminish complications, standardize approaches and solidify all practitioners of heterogeneous training. It is well-organized, salient and direct; not another device should be implanted without consideration and digestion of this necessary work.

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Comments not included in the Early View version of this paper.

