

# ASRA Pain Medicine consensus practice infection control guidelines for regional anesthesia and pain medicine

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## ABSTRACT

**Background** To provide recommendations on risk mitigation, diagnosis and treatment of infectious complications associated with the practice of regional anesthesia, acute and chronic pain management.

**Methods** Following board approval, in 2020 the American Society of Regional Anesthesia and Pain Medicine (ASRA Pain Medicine) commissioned evidence-based guidelines for best practices for infection control. More than 80 research questions were developed and literature searches undertaken by assigned working groups comprising four to five members. Modified US Preventive Services Task Force criteria were used to determine levels of evidence and certainty. Using a modified Delphi method, >50% agreement was needed to accept a recommendation for author review, and >75% agreement for a recommendation to be accepted. The ASRA Pain Medicine Board of Directors reviewed and approved the final guidelines.

**Results** After documenting the incidence and infectious complications associated with regional anesthesia and interventional pain procedures including implanted devices, we made recommendations regarding the role of the anesthesiologist and pain physician in infection control, preoperative patient risk factors and management, sterile technique, equipment use and maintenance, healthcare setting (office, hospital, operating room), surgical technique, postoperative risk reduction, and infection symptoms, diagnosis, and treatment. Consensus recommendations were based on risks associated with different settings and procedures, and keeping in mind each patient's unique characteristics.

**Conclusions** The recommendations are intended to be multidisciplinary guidelines for clinical care and clinical decision-making in the regional anesthesia and chronic interventional pain practice. The issues addressed are constantly evolving, therefore, consistent updating will be required.

## INTRODUCTION

Surgical site infection (SSI) is defined as infection of the incision, organ, or space after surgery. Surgical-related and procedural-related infections

carry significant clinical, humanistic, and economic impact. In the USA and England, SSIs are the second and third reported healthcare-related infections.<sup>1–5</sup> Unfortunately, the most recent US Centers for Disease Control (CDC) infection data from 2022 demonstrated a 4% increase in the standardized infection ratio related to all National Healthcare Safety Network (NHSN) operative procedure categories combined compared with the previous year.<sup>5</sup> In the Anesthesia Closed Claims projects database for implantable devices for chronic pain, the most common damaging events for surgical device procedures were infections.<sup>6</sup> Patients who experience SSI can suffer significant morbidity and mortality, including higher risk of long-term infection as well as death.<sup>7</sup> If left untreated, infections associated with spinal cord stimulation (SCS) have been associated with significant morbidity, including paralysis and mortality.<sup>8</sup> The economic impact of SSI is staggering: in the USA alone, the estimated additional cost for a hospital-acquired SSI is US\$28 219 (95% CI US\$18 237 to US\$38 202) and SSIs are associated with healthcare-related costs >US\$3 billion annually.<sup>9,10</sup> When examining SCS implantable pain device infections from 2009 to 2014, estimated annual healthcare expenditures for a patient with infection were US\$59 716 (95% CI US\$48 965 to US\$69 480), and only 26% of patients who were explanted for infection underwent a reimplantation.<sup>11</sup> For most patients beneficial therapy was not restored.

In 2016, WHO released two separate publications providing guidance on prevention of SSIs. Given the impact that SSIs have across the globe and the lack of international guidance, WHO provided preoperative and perioperative recommendations to prevent SSIs, as well as guidance for clinicians in the perioperative period.<sup>12,13</sup> The WHO guidelines provided a critical and unique global perspective, including the consideration of resources available in low- and middle-income countries. The CDC in 2018 released evidence-based infection guidelines, providing safe practices to be taken with all patients in orthopedic and pain management settings to



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prevent the transmission of infectious agents.<sup>14</sup> The CDC guidelines provide key recommendations for the development of infection prevention and control programs and the required infrastructure to support them.

Although approximately 50% of SSIs are thought to be preventable when evidence-based infection control practices are followed, compliance with best practices is still limited in the field of pain medicine.<sup>15</sup> An international survey on infection control practices for SCS demonstrated low compliance with evidence-based practices recommended by the CDC, the National Institute for Health and Care Excellence (NICE), and the Surgical Care Improvement Project (SCIP), and only 4 of the 15 practices had compliance rates >80%.<sup>16</sup> Two more recent surveys continue to demonstrate non-compliance with evidence-based recommendations and limited adherence to the Neuro-modulation Appropriateness Consensus Committee (NACC) infection control recommendations, including the inappropriate continuation of antibiotics in the postoperative period.<sup>17,18</sup> The risk of infection during acute and chronic pain procedures merits consideration and clinicians deserve clear recommendations for prevention and management.

Our purpose is to provide evidence-based recommendations on risk mitigation of infectious complications associated with the practice of regional anesthesia and pain management. In 2017, the American Society of Regional Anesthesia and Pain Medicine (ASRA Pain Medicine) and the American Society of Anesthesiologists (ASA) issued a practice advisory on the prevention and management of infectious complications associated with neuraxial techniques.<sup>19</sup> The scope of these current recommendations extends beyond neuraxial blocks and includes various nerve blocks (peripheral and spinal), chronic pain procedures, and minimally invasive surgical techniques used in acute and chronic pain management. Where relevant and appropriate based on current evidence, recommendations from WHO, CDC, NICE, SCIP, NACC, and other guidelines have been considered and their significance mentioned for infection prevention in practices for the operating room (OR), regional anesthesia, and interventional chronic pain management.

## METHODS AND DEVELOPMENT PROCESS

On February 7, 2020, the ASRA Pain Medicine Board of Directors commissioned a workgroup to create evidence-based guidelines concerning the best practices for limiting, diagnosing, and treating infections in both regional anesthesia and interventional pain medicine practices. Broad representation from the acute pain, regional anesthesia, and interventional pain medicine membership was sought, with particular focus on content expertise with experience in guidelines creation. As such, the ASRA Pain Medicine Infection Control Guidelines Committee was created and charged with preparing guidelines. The guidelines were meant to be a living document that would, at appropriate intervals, be updated as new information and best-practice data became available.

Questions and formats were developed by the committee chair based on recommendations from the group and were refined by a series of conference calls at regular intervals. Individual study questions were developed by individual subgroups consisting of four to five people assigned by the committee chair. One individual was assigned as the subgroup leader and that individual oversaw the question development, obtained responses, and edited the section based on the subgroup members' input. After consensus was obtained, a modified Delphi method was used to compile responses from an open discussion format that

included written responses as well as commentary from multiple consensus conference calls and emails. At the initial conference call, it was decided that >50% panel member agreement was needed to report a recommendation to the larger group, but that ≥75% agreement was required to report the recommendation in the final manuscript. Additionally, it was decided that the US Preventive Services Task Force (USPSTF) recommendation format would be used with modification for the ASRA Pain Medicine process to fit the question format.<sup>20,21</sup> After the task force completed the guidelines, the final document was sent to the ASRA Pain Medicine Board of Directors for review and approval.

At the organizational meeting, it was determined that a comprehensive search would be undertaken with studies since 1995 found in MEDLINE, Embase, Google Scholar, and the Cochrane Database of Systematic Reviews. Recognizing the significant evolution of periprocedural infection management, in order to base recommendations on current evidence, it was the consensus of the committee that literature from 1995 onward be used, with preference for recent literature. There were no limitations on language or types of articles considered. Examples of keywords used for the search for each section were "infection, antibiotics, regional anesthesia, interventional pain, spinal cord stimulation, intrathecal drug delivery (IDD), injection, epidural." The overall keyword search strategy appears in online supplemental appendix A. Given the diverse nature of the questions being asked, section authors were allowed to conduct focused searches more specific to their section content, based on the agreed-on keywords and using the same methodology as the larger committee-sponsored search. A list of abbreviations is available in online supplemental appendix B.

Statements and recommendations were created and evaluated based on the USPSTF methodologies noted in tables 1 and 2. A grade was assigned to each recommendation based on the evidence available. The level of certainty about the grade was supplied based on the available literature as outlined in table 2. The USPSTF methodology has been used in modified format by multiple societies such as ASRA Pain Medicine, American Academy of Pain Medicine, American Society of Interventional Pain Physicians, and the International Neuromodulation Society because of its flexibility and universal applicability to create highly reliable recommendations in the absence of multiple high-quality level 1 studies.<sup>22–26</sup>

The pain management procedures were classified according to the nature and risk for SSI: musculoskeletal and peripheral nerve blocks (PNBs); neuraxial and paravertebral injections; neuromodulatory, intradiscal, and minimally invasive procedures; and surgical-type interventional pain procedures (table 3).

## SURGICAL SITE INFECTION DEFINITIONS AND ASSOCIATED PATHOGENS

### Definition of a surgical site infection

An SSI is defined as an infection of the incision, organ, or space that occurs after surgery. SSIs are classified by depth and tissue spaces involved: superficial (involving the skin and subcutaneous tissues), deep (involving the fascia and muscle layers), and organ/space. An SSI is further defined as occurring within 30 (superficial SSI and deep SSI without an implant in place) to 90 (deep SSI when an implant is in place) days. Originally, the CDC had defined a deep SSI to occur within 1 year of an index surgery during which an implant was left in place.<sup>27</sup> In 2016, the CDC reduced this timeframe from within 1 year to within 90 days.<sup>5,15</sup> The CDC provides specific elements that must be met for the

**Table 1** Modified USPSTF grade criteria

Grade	Definition	Suggestions for practice
A	The ASRA Pain Medicine Infection Task Force recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The ASRA Pain Medicine Infection Task Force recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The ASRA Pain Medicine Infection Task Force recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service for selected patients depending on individual circumstances.
D	The ASRA Pain Medicine Infection Task Force recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I (Insufficient)	The ASRA Pain Medicine Infection Task Force concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the clinical considerations section of USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

ASRA, American Society of Regional Anesthesiologists; USPSTF, US Preventive Services Task Force.

definition of superficial and deep SSIs (table 4). Note that table 4 is not specific to pain procedures.

### Statements

- ▶ *Superficial SSIs involve the skin and subcutaneous tissues and exclude the fascia and muscle layers. Level of certainty: high.*
- ▶ *Deep SSIs involving an implantable device are defined as occurring within 90 days of surgery. Level of certainty: high.*

### Pathogens associated with infections

Pathogens causing SSIs can originate from either endogenous or exogenous sources with endogenous pathogens from the patient's own flora being the most common source of SSIs.<sup>28</sup> The most common pathogens associated with SSIs are *Staphylococcus aureus*, coagulase-negative *Staphylococcus* (CoNS), *Enterococcus*, *Escherichia coli*, and *Pseudomonas aeruginosa*.<sup>29</sup> It has been shown that 80%–85% of SSIs resulting from *S. aureus* match cultures from the patient's nares.<sup>30</sup> Between 0.84% and 7% of patients screen positive for methicillin-resistant *S. aureus*

(MRSA) and >30% of non-institutionalized people in the USA are colonized with methicillin-susceptible *S. aureus* (MSSA).<sup>31–34</sup> A recent study examining the prevalence of *S. aureus* colonization in SCS patients demonstrated that colonization was present in >20% of cases, with MSSA carriage occurring at a rate nearly five times that of MRSA.<sup>35</sup> Furthermore, MRSA screening alone failed to identify >90% of *S. aureus*-colonized patients with only MSSA carrier status. Colonization with MSSA or MRSA is associated with a higher risk of SSI and of morbidity and mortality from SSIs.<sup>31–34</sup> Approximately two-thirds of implantable device infections are caused by *S. aureus* or CoNS.<sup>36</sup> Staphylococci are frequent sources of biofilm, which forms a physical barrier against antibodies and granulated cell populations that impedes the penetration of antibiotics. *S. aureus* biofilm-associated implant infections are difficult to treat with antibiotics, increase the development of antimicrobial resistance, and often necessitate implant removal.

The most common colonizing organisms are the skin commensals: the CoNS, with *Staphylococcus epidermidis* the most

**Table 2** USPSTF levels of certainty regarding net benefit\*

Level of certainty	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies. Examples—RCTs or large-scale observational studies with control groups.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by such factors as: <ul style="list-style-type: none"> <li>▶ The number, size, or quality of individual studies.</li> <li>▶ Inconsistency of findings across individual studies.</li> <li>▶ Limited generalizability of findings to routine primary care practice.</li> <li>▶ Lack of coherence in the chain of evidence.</li> </ul> As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion. Examples—a single large-scale observational study without control groups (multisite or single-site); multiple (>2) large retrospective studies (>20 subjects) or cohort studies.
Low	The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of: <ul style="list-style-type: none"> <li>▶ The limited number or size of studies.</li> <li>▶ Important flaws in study design or methods.</li> <li>▶ Inconsistency of findings across individual studies.</li> <li>▶ Gaps in the chain of evidence.</li> <li>▶ Findings not generalizable to routine primary care practice.</li> <li>▶ Lack of information on important health outcomes.</li> </ul> More information may allow estimation of effects on health outcomes. Examples—case series or case reports or consensus-based recommendations from other sources.

\*The USPSTF defines certainty as 'likelihood that the USPSTF assessment of the net benefit of a preventive service is correct.' The net benefit is defined as benefit minus harm of the preventive service as implemented in a general, primary care population. The USPSTF assigns a certainty level based on the nature of the overall evidence available to assess the net benefit of a preventive service.

RCT, randomized controlled trial; USPSTF, US Preventive Services Task Force.

**Table 3** Pain procedure classifications to guide infection control measures

A (Musculoskeletal and PNBs)	B (Neuraxial and paravertebral procedures, sympathetic blocks)	C (Neuromodulation, intradiscal, and minimally invasive procedures)	D (Surgical-type interventional pain procedures)
Trigger point injections	Epidural corticosteroid injections (interlaminar and transforaminal)	Intradiscal procedures	Peripheral nerve stimulation implants/replacements/revisions
Musculoskeletal and joint injections	Facet joint and medial branch nerve block injections and radiofrequency ablation	Peripheral nerve stimulation trials	Spinal cord stimulation implants/replacements/revisions
Single-injection PNBs	Sacroiliac joint injections and sacral lateral branch blocks and radiofrequency ablation	Spinal cord stimulation trials	Dorsal root ganglion stimulation implants/replacements/revisions
	Paravertebral blocks	Dorsal root ganglion stimulation trials	Interspinous spacer/fusion implants
	Sympathetic blocks (stellate, splanchnic, celiac, lumbar, superior hypogastric, ganglion impar)	Vertebral augmentation (vertebroplasty and kyphoplasty)	Intrathecal catheter and pump implants/replacements/revisions
	Single-injection intrathecal drug trials	Percutaneous image-guided lumbar decompression	Sacroiliac joint fusion
	Intrathecal pump refills	Basivertebral nerve ablation	
	Indwelling catheters ≤4 days (peripheral, epidural, intrathecal)	Indwelling catheters >4 days (peripheral, epidural, intrathecal)	

PNB, peripheral nerve block.

frequently isolated organism, followed by other skin commensals including *Pseudomonas* spp, *Corynebacterium*, *S. aureus*, enterococci, and Gram-negative organisms (*E. coli*, *Acinetobacter*, *Klebsiella*, micrococci, *Sphingomonas*).<sup>37–44</sup> Epidural abscesses are most commonly associated with *S. aureus* followed by *Pseudomonas* spp.<sup>45–53</sup> With respect to meningitis following neuraxial blocks, a pooled analysis of case reports noted that oral commensals (eg, *Streptococcus salivarius*) are the most common bacteria (17.0%) related to spinal anesthesia, followed by *Serratia marcescens* (8.5%) and *Pseudomonas* spp (9.9%), while it was *S. aureus* (26.7%) that was the most common organism causing meningitis following epidurals.<sup>54</sup> A similar report by Moen *et al* also noted that epidural abscesses were commonly due to staphylococci, while beta-hemolytic streptococci were commonly associated with meningitis following single-shot spinal procedures.<sup>48</sup>

#### Statements

- ▶ *S. aureus* is the most common pathogen associated with implantable pain therapies SSIs. Level of certainty: high.
- ▶ *S. aureus* colonization confers increased risk of infection for implanted devices. Level of certainty: moderate.

### INFECTION RATES OF REGIONAL ANESTHESIA AND INTERVENTIONAL PAIN PROCEDURES

The incidence of infections from regional anesthesia and interventional pain procedures is difficult to discern based on the available literature, which often consists of sporadic case reports or small series.<sup>28 55–61</sup> Large longitudinal cohort studies have shown continuous epidural anesthesia to be associated with a higher risk of infection compared with spinal anesthesia<sup>62</sup>; however, serious infections have also occurred following combined epidural-spinal and spinal procedures.<sup>53 63 64</sup> Breaches in aseptic technique are implicated in most cases, but causes likely are multifactorial. A summary of the descriptions and rates of infection following specific interventional pain procedures follows.

#### Trigger point injections

Trigger point injections (TPIs) involve deposition of local anesthetic with or without corticosteroid into taut bands of muscle tissue characterized clinically as ‘trigger points,’ particularly

common in myofascial pain syndrome. Although these procedures are generally considered very safe, infections do occur and have been reported in the literature,<sup>65 66</sup> particularly when proper infection-control practices are not followed.<sup>67</sup> The incidence of infection following TPIs has not been reported, due to the rarity of this complication.

#### Musculoskeletal joint injections

Most of the literature concerning joint infection following intra-articular corticosteroid (IACS) injection focuses on risk relative to the timing of joint replacement surgery. The incidence of infection following IACS into native joints is not well-reported, aside from reports of infection outbreaks related to contamination largely due to suboptimal infection control practices. The incidence of septic arthritis following major joint injections has been reported to be 0.03%–0.08%.<sup>68 69</sup>

A single-center retrospective review of 69 450 joint injections/aspirations identified only four cases of septic arthritis with a history of infection in the affected joint within the past 90 days.<sup>70</sup> All four cases involved native joints (one shoulder, three knee joints); one joint had gadolinium contrast injected, and the other three had injection of corticosteroid (triamcinolone) with bupivacaine. Patients presented with symptoms including pain, fever, swelling/effusion, and reduced range of motion of the affected joint. Reported inflammatory markers included white blood cells (WBCs, 10–18.3 k/μL), erythrocyte sedimentation rate (ESR, 7.2–40 mm/hour), and C reactive protein (CRP, 2.4–20.4 mg/dL) as well as synovial fluid analysis with polymorphonuclear cells (29 000–182 800 k/μL; 78%–96%). Time from injection to presentation ranged from 2 to 5 days (median 3 days). Cultured bacteria included *Streptococcus sanguinis* (n=1), *Abiotrophia defectiva* (n=1), and *Streptococcus mitis/oralis* (n=2). All patients were males, ages ranging from 63 to 76 years. Treatment included irrigation and debridement with at least 4 weeks of parenteral antibiotic therapy; one patient required a second irrigation and debridement, and another required an additional 6 weeks of antibiotic therapy for recurrence of infection.

The effect of IACS injection on the risk of prosthetic joint infection (PJI) following joint replacement surgery has been well studied, largely with retrospective cohort studies. A

**Table 4** 2024 Centers for Disease Control (CDC) National Healthcare Safety Network (NHSN) surgical site infection (SSI) checklist<sup>5</sup>

Superficial incisional SSI	
Criteria	<p>Date of event occurs within 30 days following the NHSN operative procedure (where day 1=the procedure date)</p> <p>AND</p> <p>involves only skin and subcutaneous tissue of the incision</p> <p>AND</p> <p>patient has at least one of the following:</p> <ol style="list-style-type: none"> <li>purulent drainage from the superficial incision</li> <li>organism(s) identified from an aseptically obtained specimen from the superficial incision or subcutaneous tissue by a culture or non-culture-based microbiological testing method which is performed for purposes of clinical diagnosis or treatment (eg, not active surveillance culture/testing)</li> <li>a superficial incision that is deliberately opened by a surgeon, physician,* or physician designee and culture-based or non-culture-based testing of the superficial incision or subcutaneous tissue is not performed</li> </ol> <p>AND</p> <p>patient has at least one of the following signs or symptoms: localized pain or tenderness; localized swelling; erythema; or heat</p> <p>d. Diagnosis of a superficial incisional SSI by a physician* or physician designee</p>
Comments	<p>There are two specific types of superficial incisional SSIs:</p> <ol style="list-style-type: none"> <li>Superficial incisional primary: a superficial incisional SSI that is identified in the primary incision in a patient that has had an operation with one or more incisions (eg, cesarean section incision or chest incision for CBGB (both chest and donor site incisions)).</li> <li>Superficial incisional secondary: a superficial incisional SSI that is identified in the secondary incision in a patient that has had an operation with more than one incision (eg, donor site incision for CBGB).</li> </ol> <p>Note: Refer to SSI Event Reporting Instruction #7** for NHSN operative procedure categories with secondary incision sites available for SSI attribution.</p>
Reporting instructions for superficial incisional SSI	<p>The following do not qualify as criteria for meeting the NHSN definition of superficial incisional SSI:</p> <ul style="list-style-type: none"> <li>▶ Diagnosis/Treatment of cellulitis (redness/warmth/swelling), by itself, does not meet superficial incisional SSI criterion 'd.'</li> <li>▶ A stitch abscess alone (minimal inflammation and discharge confined to the points of suture penetration).</li> <li>▶ A localized stab wound or pin site infection; depending on the depth, these infections might be considered either a skin (SKIN) or soft tissue (ST) infection.</li> </ul> <p>Notes:</p> <ul style="list-style-type: none"> <li>▶ For the purpose of NHSN surveillance, the term 'incision' refers to the incision made for the primary surgical procedure and the term 'stab wound' refers to an incision made at another site, generally to accommodate a drain.</li> <li>▶ For an NHSN operative procedure, a laparoscopic trocar site is considered a surgical incision and not a stab wound. If a surgeon uses a laparoscopic trocar site to place a drain at the end of a procedure, this is considered a surgical incision.</li> </ul>
Deep incisional SSI	
Criteria	<p>Date of event occurs within 30 or 90 days following the NHSN operative procedure (where day 1=the procedure date) according to the list in <a href="#">table 2</a></p> <p>AND</p> <p>involves deep soft tissues of the incision (eg, fascial and muscle layers)</p> <p>AND</p> <p>patient has at least one of the following:</p> <ol style="list-style-type: none"> <li>purulent drainage from the deep incision</li> <li>a deep incision that is deliberately opened or aspirated by a surgeon, physician,* or physician designee or spontaneously dehisces</li> </ol> <p>AND</p> <p>organism(s) identified from the deep soft tissues of the incision by a culture or non-culture-based microbiological testing method which is performed for purposes of clinical diagnosis or treatment (eg, not active surveillance culture/testing) or culture-based or non-culture-based microbiological testing method is not performed. A culture-based or non-culture-based test from the deep soft tissues of the incision that has a negative finding does not meet this criterion</p> <p>AND</p> <p>patient has at least one of the following signs or symptoms: fever (&gt;38°C); localized pain or tenderness</p> <p>c. an abscess or other evidence of infection involving the deep incision detected on gross anatomical exam, histopathological exam, or imaging test</p>
Comments	<p>There are two specific types of deep incisional SSIs:</p> <ol style="list-style-type: none"> <li>Deep incisional primary: a deep incisional SSI that is identified in a primary incision in a patient that has had an operation with one or more incisions (eg, cesarean section incision or chest incision for CBGB)</li> <li>Deep incisional secondary: a deep incisional SSI that is identified in the secondary incision in a patient that has had an operation with more than one incision (eg, donor site incision for CBGB)</li> </ol> <p>Note: Refer to SSI Event Reporting Instruction #7** for NHSN operative procedure categories with secondary incision sites available for SSI attribution.</p>
<p>**Adapted from the NHSN, CDC. SSI event. January 2024. Accessed January 27, 2024. Note that this table is not specific to pain procedures. Please consult the CDC website for complete details, such as reporting instructions for operative procedure categories and secondary incision sites, referred to by #7 in the table above: <a href="https://www.cdc.gov/nhsn/pdfs/pscmanual/9pscscscurrent.pdf">https://www.cdc.gov/nhsn/pdfs/pscmanual/9pscscscurrent.pdf</a>.</p> <p>*The term physician for the purpose of application of the NHSN SSI criteria may be interpreted to mean a surgeon, infectious disease physician, emergency physician, other physician on the case, or physician's designee (nurse practitioner or physician's assistant).</p> <p>CBGB, coronary artery bypass graft with both chest and donor site incisions.</p>	

meta-analysis of 11 cohort studies assessing PJI risk following total knee arthroplasty (TKA) and total hip arthroplasty (THA) found an increased risk of PJI in patients who had received IACS to the affected joint (RR 1.436; 95% CI 1.085 to 1.900) with moderately high heterogeneity among studies (12=53.5%;  $p=0.022$ ).<sup>71</sup> An earlier meta-analysis of eight studies measured PJI incidence following TKA and THA in patients undergoing IACS prior to surgery and found a low level of certainty in the evidence (Grading of Recommendations, Assessment, Development and Evaluations criteria)<sup>72</sup> and that preoperative IACS to the affected joint resulted in a higher rate of deep SSI (OR 2.13, 95% CI 1.02 to 4.45).<sup>73</sup> A second contemporaneous meta-analysis found that there was no increased incidence of SSI

associated with IACS to the affected joint prior to THA or TKA; however, none of the six included studies reported IACS administered within 3 months prior to surgery.<sup>74</sup> Yet another meta-analysis published during the same year found no association between preoperative IACS injection and SSI following THA or TKA, although again the injections were not stratified according to length of time between injection and surgery and most studies did not include IACS injections administered within 3 months of joint replacement.<sup>75</sup> Earlier meta-analyses and narrative reviews also maintained no clear relationship between IACS and PJI following joint replacement surgery, with included studies lacking clear data regarding timing of injection prior to operation.<sup>76,77</sup>

Studies have demonstrated an increased risk of PJI with ICS to the index joint performed within 3 months before TKA. A retrospective study of a national private insurance database involving 58 337 patients who underwent TKA found an increased risk of PJI with injection of both corticosteroid (OR 1.21,  $p=0.014$ ) and hyaluronic acid (OR 1.55,  $p=0.029$ ) when administered within 3 months of TKA, with no significant difference in risk between the two types of injection.<sup>78</sup> A national database study of 76 090 patients showed increased risk when the injection is done within 1 month prior to TKA.<sup>79</sup> Elevated rate of infection following TKA was associated with preoperative IACS injection when administered up to 6 months prior to surgery in a review of private insurer database records from 2007 to 2014, including a total of 83 684 TKA surgeries.<sup>80</sup> One exception is a retrospective cohort study of 302 patients who had undergone IACS injection prior to TKA, matched with controls undergoing TKA without prior IACS injection, which did not find any increased incidence associated with injection administered from 10 weeks to >12 months prior to TKA.<sup>81</sup> Increased risk of knee PJI was found to be associated with intraoperative IACS injection of the affected joint in a national Medicare database review including 2866 patients undergoing IACS injection at time of TKA compared with 170 350 matched controls at 3 months (0.66% vs 0.25%, OR 2.6,  $p<0.0001$ ) and 6 months (1.92% vs 0.54%, OR 3.6,  $p<0.0001$ ).<sup>82</sup> Studies have also demonstrated elevated risk of periprosthetic infection with IACS administered following TKA.<sup>83</sup> A retrospective chart review identifying 736 patients who underwent ipsilateral knee injection following TKA identified an acute (within 3 months) infection rate of 0.16%.<sup>84</sup> Interestingly, IACS injection given intraoperatively does not appear to increase the rate of postoperative joint infection, possibly related to the sterile environment.<sup>85</sup>

A retrospective study assessing the rate of prosthetic hip joint infection in 350 patients who underwent single intra-articular hip joint injection compared with 106 patients who received multiple intra-articular hip joint injections in the 12 months prior to THA found that the single-injection cohort had an infection rate of 2.0% compared with the multiple-injection cohort of 6.6% ( $p=0.04$ , OR 3.30).<sup>86</sup> The authors found no difference between the cohorts in terms of age, gender, ASA score, history of diabetes mellitus or body mass index (BMI). The query of a Medicare-based insurance database found an increased incidence of PJI following THA in patients who underwent hip joint IACS injection within 3 months prior to surgery (incidence at 3 months post-THA 2.41%, OR 1.9,  $p=0.004$ ; incidence at 6 months 3.74%, OR 1.5,  $p<0.019$ ).<sup>87</sup> Another review of state-level ambulatory surgery and inpatient databases also found increased incidence of PJI following THA in patients who received hip joint IACS within 3 months prior to surgery compared with patients who did not receive IACS before surgery. The increased incidence was noted postsurgery at 3 months (1.58% vs 1.04%,  $p=0.015$ ), at 6 months (1.76% vs 1.21%,  $p=0.022$ ), and at 1 year (2.04% vs 1.47%,  $p=0.031$ ), respectively. There was no association with increased incidence of PJI in patients who received IACS >3 months prior to surgery.<sup>88</sup>

Ipsilateral shoulder injection of corticosteroid within 1 month following shoulder surgery was found to be associated with increased risk of postoperative infection in a study involving 3946 patients obtained from a private payer and Medicare national database (private payer, OR 2.63 ( $p=0.014$ ), Medicare, OR 11.2, ( $p<0.0001$ )).<sup>89</sup> A similar association was found between corticosteroid injection administered within 1 month prior to arthroscopic rotator cuff repair (OR 1.7 [95% CI 1.0 to 2.9,  $p=0.04$ ]) in a national private payer database involving

60 823 patients, 19.8% of whom received a shoulder injection within 1 year prior to surgery.<sup>90</sup> A review of a national Medicare database found increased incidence of infection at 3 months (OR 2.0,  $p=0.07$ ) and 6 months (OR 2.0,  $p=0.001$ ) following shoulder arthroplasty with IACS injection performed within 3 months prior to surgery.<sup>91</sup>

Certain comorbidities increase the risk of native joint infection following IACS injection. A case-control study (50 patients with knee infection following IACS injection [with corticosteroid or hyaluronic acid] matched with 250 non-infected controls who had received IACS injection) identified increased risk of knee infection within 6 months following IACS injection associated with BMI >25 kg/m<sup>2</sup> (OR 2.3, 95% CI 1.1 to 4.7), injection of corticosteroid compared with hyaluronic acid (OR 3.21, 95% CI 1.63 to 6.31), rheumatoid arthritis (OR 2.61, 95% CI 1.20 to 5.68), and injection performed by a general practitioner rather than an orthopedic surgeon (OR 5.23, 95% CI 2.00 to 13.67).<sup>92</sup> Patients with presentation of septic arthritis within 2 weeks following injection were more likely to experience fever, erythema, swelling, rest pain, night pain, limited range of motion, elevated WBC, and elevated CRP than patients with chronic low-grade infection (presenting >2 weeks following injection). The development of several cases of septic knee arthritis prompted an investigation of a private pain clinic by the New Jersey Department of Public Health, identifying 41 cases of intra-articular knee injection-associated septic arthritis associated with multiple breaches of recommended infection practices and standard aseptic technique.<sup>93</sup> The most commonly cultured organism in acute cases was *S. aureus* (47.6%) followed by *Streptococcus* spp, *Enterococcus* spp, and Gram-negative bacilli (each 9.5%). The most commonly cultured organism in chronic cases was CoNS (31.0%), followed by *S. aureus* and *Propionibacterium acnes* (each 24.1%), and Gram-negative bacilli (10.3%).

An increased rate of infection has also been found to be associated with IACS injection at the time of ankle arthroscopy compared with patients who did not receive local IACS injection (OR 2.2, 95% CI 1.4% to 3.7%,  $p=0.002$ ), independent of age, gender, smoking status, obesity, and Charlson Comorbidity Index.<sup>94</sup>

### Sacroiliac joint injections

The rate of infection following sacroiliac joint (SIJ) infections is unknown, with several case reports in the literature including significant morbidity associated with injections administered in immunocompromised patients and injections performed without adherence to best practices for medication vial management.<sup>95–97</sup> Despite SIJ being a very common procedure, no studies exist investigating the incidence of SIJ infection following IACS injection.

### Neuraxial and paravertebral injections in chronic pain management

This section refers to neuraxial and paravertebral injections deployed in chronic pain management, including intrathecal and epidural injections and implantable pain therapies. The estimated incidence of central nervous system (CNS) infections following paraspinal therapy is 1/1000 (0.1%).<sup>33</sup> However, when separating out specific paraspinal injections, it is difficult to discern the true incidence related to each procedure. The risk of developing an epidural abscess from an indwelling epidural catheter has been reported to be 1/1930 (0.05%).<sup>51</sup> Lee *et al* published data on 5 015 09 patients undergoing single-shot

epidural injections and found an incidence of 0.01% within 90 days postinjection.<sup>98</sup>

An outbreak of *S. marcescens* infections following neuraxial procedures at a single pain clinic identified the likely source to be single-use contrast vials that were used for multiple patients.<sup>57</sup> This and other reports of localized infectious outbreaks highlight the risks of infection when proper infection-control practices are not followed, including in preparation of injected medication, which elevates the risk of infection beyond that expected when standard operating procedures are followed.<sup>99</sup>

The incidence of infection following epidural corticosteroid injection (ESI) has been stratified primarily in the surgical literature with respect to timing of spine surgery, chiefly whether ESI prior to spine surgery increases risk of SSI. Although there are several reports of outbreaks of infection following use of contaminated vials of medication, the overall incidence of infection following ESI is low, with few studies citing population-based incidence. Limited studies have estimated the incidence to be 1%–2%, with severe infection following ESI occurring rarely, in <1/10 000 injections.<sup>100 101</sup> With only a single study reporting incidence of infection following ESI and no recent studies reporting population-level incidence, the level of certainty in incidence estimates is low. The following studies characterize the debate between ESI administration and increased risk of SSI following spine surgery.

An updated review of risks associated with ESIs compared reported complications and risks from cervical and lumbar transforaminal ESIs.<sup>102</sup> Major reported complications in 2017–2018 from cervical ESIs included primarily neurological injury resulting from bleeding events and/or intra-arterial or intramedullary injection. One documented case involved cervical epidural abscess occurring after two insertions of an epidural catheter at the C7-T1 interspace for administration of corticosteroid, spaced 24 hours apart, for treatment of neck pain and radiculopathy occurring from disc herniation.<sup>103</sup> Of note, the patient had developed lesions consistent with acute herpes zoster infection and had commenced antiviral therapy 24 hours prior to administration of the first ESI. The patient developed myalgias, weakness, headache, fatigue, and low-grade fever (37.8°C), with elevated WBC count of 24.27 k/μL (neutrophils 92.41%), ESR of 66 mm/hour, and CRP of 193.8 mg/L. The patient was started on parenteral antibiotic due to suspected cervical epidural abscess, with MRI subsequently confirming epidural abscess from C6 to T8. The patient remained hospitalized for over 1 month for treatment with intravenous antibiotics (vancomycin 1 g every 12 hours, imipenem/cilastatin sodium 1 g every 8 hours) and ongoing antiviral therapy, with resolution of symptoms and without any evidence of infection on follow-up MRI. The patient did not undergo surgical irrigation and debridement. In addition to describing the classic symptoms of spinal epidural abscess (SEA), including neck/back pain, fever, and neurological deficits, the authors noted the patient's likely immunocompromised status in the setting of active zoster infection.

A single-center retrospective study assessing rate of SEA over an 11-year period found an incidence of 5.1 cases for every 10 000 admissions, 52% of which identified routes of infection including bacteremia (26%), recent surgery/procedure (21%), and injection (6%).<sup>104</sup> Almost all the injection-related cases had involved a spinal injection; one injection-related case was a kyphoplasty. Most of the SEA cases were associated with *S. aureus* (84%) followed by other Gram-positive cocci (14%), Gram-negative cocci (5%), and one case each involving *Brucella* and *P. acnes*. All patients were treated with parenteral antibiotic therapy, and 73% required surgical irrigation and debridement.

Only 8% of patients presented with all three classical symptoms of SEA (spinal pain, fever, neurological deficit). Only 56% of patients demonstrated leukocytosis, but ESR and CRP were elevated in almost all subjects (97% and 98%, respectively). Overall, 15% of patients experienced persistent adverse outcomes including neurological deficits (8%) and death (7%).

A prospective observational study assessing systemic reactions reported by patients within 2 weeks following ESI in 960 cases (885 patients) did not identify any patients who developed symptoms concerning for infection.<sup>105</sup> A single-site prospective observational study, including a total of 10 261 epidural procedures over a period of 20 months, identified no cases of infection following ESI; however, formal follow-up was limited to a 48-hour period following injection.<sup>106</sup>

Much of the literature concerns the risk of perioperative administration of ESIs. One retrospective cohort study involving 3403 patients in the Military Health System found no elevated risk of postoperative infection in patients who had received lumbar ESI prior to lumbar arthrodesis.<sup>107</sup> A second retrospective study including 15 011 patients found an increased risk of infection among patients who received ESI prior to fusion surgery, but not prior to decompression surgery (2.68% vs 1.69%,  $p=0.025$ ).<sup>108</sup> A comparative prospective study enrolling 2312 patients found a higher rate of postoperative infection in patients receiving lumbar ESI within 1 month prior to lumbar surgery but not in patients who received lumbar ESI >1 month prior to surgery compared with patients who did not receive lumbar ESI (6.98% in the ESI within 30 days group compared with 3.51% in the control group, OR 1.99, 95% CI 1.21 to 3.22,  $p=0.01$ ).<sup>109</sup> A 10-year retrospective review assessing association of preoperative ESI with SSI following lumbar spine surgery in 5311 patients did not find increased incidence of SSI associated with preoperative SSI (OR 0.67, 95% CI 0.27 to 1.64,  $p=0.376$ ).<sup>110</sup>

A national insurance database review assessing the association between preoperative cervical epidural corticosteroid injection (CESI) and both anterior cervical discectomy and fusion (ACDF) and posterior cervical fusion (PCF) found a significant association between CESI performed within 3 months (OR 2.21,  $p<0.0001$ ) and within 3–6 months (OR 1.95,  $p=0.0002$ ) prior to PCF and development of postoperative infection. For patients undergoing ACDF, CESI within 3 months was associated with increased rate of postoperative infection (OR 1.83,  $p<0.0001$ ).<sup>111</sup>

The most devastating series of events associated with infection following ESI is well-documented and associated with preservative-free methylprednisolone acetate from a single compounding pharmacy contaminated with fungi, including primarily *Exserohilum rostratum* as well as the non-pathogenic *Rhodotorula laryngis* and *Rhizopus stolonifer*.<sup>112 113</sup> The contaminated corticosteroid was contained in 17 675 vials distributed to 76 facilities in 23 states involving potential exposure of up to 13 534 patients, 89% of whom had been potentially exposed through epidural, spinal, or paraspinal injections.<sup>114</sup> Nearly 750 cases of infection were reported, with presentations including spinal or paraspinal infections (43%), meningitis (31%), meningitis with spinal or paraspinal infection (20%), stroke due to meningitis (1%), and spinal or paraspinal infections along with peripheral joint infection (<1%). Overall, at least 61 deaths were attributed to the outbreak. Most were treated with antifungal therapy without known long-lasting sequelae. This incident continues to serve as a strong warning against contamination of medication administered in the neuraxis.<sup>114</sup>

Another outbreak involving eight cases of MSSA infections, including bacteremia, epidural abscess, and meningitis, was

linked to lumbar ESIs administered at a single clinic.<sup>115</sup> Procedural assessment at this site identified practices that may have led to increased risk of infection, including proceduralists not wearing masks, inconsistencies in sterile preparation, such as use of non-sterile gauze, using single-use vials of medication for multiple patients, and lack of staff awareness regarding official standard operating procedures for sterile procedural practice.

### Facet procedures including medial branch blocks

Cases of paraspinal abscesses and septic arthritis have been reported following facet joint injections, but the actual incidence has not been published.<sup>116–121</sup> A retrospective review of 11980 facet joint injection procedures in 6066 patients identified eight spine infections including one case of disseminated fungal spondylitis in a patient who had previously been treated for *Aspergillus* endophthalmitis and pulmonary aspergillosis (incidence of 0.07%). Four patients were immunocompromised.<sup>122</sup> At least one patient who received a facet joint injection experienced a localized soft tissue infection in a randomized controlled trial (RCT) involving 229 participants that compared the effectiveness of pain relief and prognostic yield for responsiveness to radiofrequency ablation (RFA) among intra-articular facet joint injection with corticosteroid, medial branch nerve blocks, and saline.<sup>123</sup> Case reports of facet joint procedures complicated by infection have described localized infection of the facet joints treated with intravenous antibiotics with and without requiring surgery,<sup>124</sup> development of epidural and spinal abscess systemic infection following facet joint injection ultimately resulting in death,<sup>125</sup> and joint infection occurring in patients without known risk factors.<sup>77 121</sup>

A prospective observational study on 7842 facet joint block episodes (both diagnostic and therapeutic) administered over a period of 20 months reported no evidence of infection in a formal follow-up period of 48 hours postprocedure.<sup>126</sup>

### Radiofrequency ablation

Infection following medial branch RFA is rare, but questionable cases of infection have been reported along with the recommendation to differentiate infection from possible soft tissue necrosis that is expected to occur after radiofrequency lesioning.<sup>127</sup> In a retrospective review comprising 616 lumbar RFA lesions in 92 patients, no cases of infection were identified.<sup>128</sup>

No studies have reported incidence of infection following sacroiliac lateral branch RFA, nor are there case reports describing such infections.

A systematic review including five high-quality and two moderate-quality RCTs did not identify any serious adverse events involving infection related to RFA of the knee for the indication of osteoarthritis.<sup>129</sup> There are no studies reporting incidence of infection following peripheral joint RFA of the hip, knee, or shoulder, but case reports describe septic arthritis following knee (genicular nerve) RFA.<sup>130 131</sup>

### Disc access

The incidence of disc infection following discography has been estimated to be 0.15% per patient and 0.08% per disc injected.<sup>132</sup> The report of a case involving a female patient who underwent L5-S1 intradiscal platelet-rich plasma (PRP) injection without intradiscal antibiotic administration describes development of *Cutibacterium acnes* spondylodiscitis within 10 weeks following the procedure and requiring 6 weeks of treatment with intravenous antibiotics (ceftriaxone 2 g/day).<sup>133</sup> The patient's presentation included night sweats and difficulty ambulating, with

normal complete blood count (CBC) with differential, ESR 9 mm/hour and CRP 39.3 mg/L. One case report described the development of discitis despite use of intradiscal antibiotics and of a two-needle technique in a patient undergoing four-level lumbar discography, requiring at least 6 weeks of parenteral antibiotic treatment.<sup>134</sup> A single prospective, double-blind RCT involving 29 patients undergoing intradiscal PRP injection with 18 patients in the control group did not identify a single case of infection through 1-year follow-up.<sup>135</sup>

The rate of discitis following cervical discography injection is rare and has been estimated to be 0.15% based on a meta-analysis of 14 studies involving a total of 14 133 disc injections.<sup>136</sup> Earlier estimates suggested an overall per-patient incidence of 0.15% and per-disc incidence of <0.08%.<sup>28 132</sup> The incidence of discitis overall varies widely, from 0% to 4.9% per patient or 0% to 1.3% per disc accessed.<sup>137</sup> The risk of infection following disc entry is rare but likely increases with multilevel disc entry.

### Needle technique recommendations for disc entry

The double-needle technique consists of placing a larger caliber introducer needle through the skin and then placing a smaller needle through it to enter the disc. Since the smaller needle passes through the larger needle without direct skin penetration, theoretically the chance of bacterial contamination of the disc access needle is reduced.

Based on a retrospective review from Fraser *et al*, a stylet, double-needle technique mitigates the rate of discitis.<sup>138</sup> The authors reported a 2.7% incidence of discitis using an 18-gauge, single-needle, non-stylet technique, which decreased to 0.7% using a stylet double-needle technique when performing lumbar discography.

The use of a stylet needle itself may be the reason for the decreased incidence of infection rather than the double-needle technique. Pobiell *et al* reported a 0.019% incidence (12 634 subjects) of discitis following cervical, thoracic, and lumbar discographies using a stylet single-needle technique.<sup>139</sup> Additionally, a meta-analysis by Kapoor *et al* of cervical discography demonstrated postprocedural discitis in 22 of 14 133 disc injections (0.15%) and 21 of 4804 patients (0.44%), and all of the studies contained in this meta-analysis either had unreported numbers of needles used or just a single needle.<sup>136</sup> These numbers are lower than the 0.7% discitis rate reported by Fraser *et al*.<sup>138</sup> The two largest contributions to the data from this meta-analysis are from Pobiell *et al*<sup>139</sup> and Zeidman *et al*.<sup>140</sup> Both studies used stylet needles, and these two studies contributed 71.6% of the subjects to the meta-analysis.

### Vertebral augmentation

The incidence of infection following vertebral augmentation has been reported to be 0.35%–0.46%.<sup>141 142</sup> No population-based or large-scale studies have reported the incidence of infection following kyphoplasty for osteoporotic compression fractures, however, it is thought to be rare, with one prospective observational study finding a per-patient incidence of 1.96%.<sup>143</sup> A retrospective case series of 11 patients who developed spinal infection following percutaneous vertebroplasty or kyphoplasty described an incidence of infection of 0.36% (in 826 cases).<sup>142</sup> Patients presented with neurological deficits, underwent immediate culture and biopsy and required both surgical and long-term antibiotic treatment. A case series of nine patients who developed pyogenic spondylitis or spondylodiscitis following kyphoplasty or vertebroplasty identified an overall rate of infection

following vertebral augmentation of 1 in 200 patients in a single practice.<sup>141</sup> Almost all patients had comorbidities putting them at elevated risk for infection, including diabetes, obesity, urinary tract infection, history of bacteremia, alcoholism, or undergoing chemotherapy. All cases used polymethylmethacrylate.

Spinal tuberculosis (TB) is an extremely rare but highly morbid infection known to occur after vertebral augmentation particularly in immunocompromised patients. Spinal TB has been reported to occur up to 1 year after kyphoplasty, and when reported, has been associated with risk factors such as advanced age and immunocompromise. Spinal TB following vertebral augmentation can occur due to hematogenous spread of active infection, local re-activation of latent infection, or can possibly be misdiagnosed as an osteoporotic compression fracture, and the authors reiterated the importance of a detailed history, careful study of advanced imaging studies to differentiate between spinal TB and compression fracture.<sup>87</sup>

The incidence of infection following vertebral augmentation may not be a straightforward calculation, partly due to delayed infection. The description of four cases of delayed pyogenic spondylitis following vertebral augmentation (mean onset of symptoms 12.3 months) included a report of overall incidence of postoperative pyogenic spondylitis following vertebral augmentation of 1.9%.<sup>144</sup> Three of the four patients had risk factors including metastatic cancer, poorly controlled diabetes mellitus, and immunocompromised status.

### Implanted or indwelling pain devices

Infection rates following SCS implantation have improved in recent years, with recent reports ranging from 2.4% to 3.1%,<sup>11 145–147</sup> and results from a large US database demonstrating a 12-month device-related infection rate of 3%.<sup>145</sup> Infection rates associated with SCS trials are typically low in trials of 10 days or less.<sup>148</sup> Infection rates associated with IDD range from 2.5% to 9%.<sup>149</sup> The improvement in infection rate is thought to be due to improved surgical technique and better understanding of best practices to prevent infection.<sup>150</sup> Nevertheless, the development of infection is among the most dreaded of complications related to implantable devices, resulting in incremental costs related to infected SCS of approximately US\$60 000 per device compared with SCS implants not complicated by infection.<sup>11</sup>

### Statements

- ▶ *The incidence of infection following TPIs is rare. Level of certainty: high.*
- ▶ *For TPIs there are case reports demonstrating rare, potentially serious infection-related complications particularly when standard infection control measures are not followed. Level of certainty: high.*
- ▶ *The incidence of infection following intra-articular injection into a native joint is rare. Level of certainty: high.*
- ▶ *The incidence of SSIs following knee replacement surgery in patients receiving IACS injection preoperatively may be increased if administered within 3 months prior to surgery. Level of certainty: moderate.*
- ▶ *There is an increased risk of postoperative deep joint infection when IACS injection is administered within 1 month prior to index joint replacement surgery. Level of certainty: moderate.*

- ▶ *The risk of PJI following shoulder surgery is elevated in patients receiving index joint IACS injection within 3 months prior to surgery. Level of certainty: moderate.*
- ▶ *Risk factors for native joint infection following IACS injection include elevated BMI >25 kg/m<sup>2</sup>, rheumatoid arthritis, and injections performed by general practitioners. Level of certainty: moderate.*
- ▶ *The incidence of infection following sacroiliac IACS injection is unknown. Rare cases have been reported typically associated with administration to immunocompromised patients or lack of adherence to infection-control practices. Level of certainty: moderate.*
- ▶ *Incidence of infection following facet joint procedures ranges from 0% to 0.07%. Infection is rare but can be life-threatening. Level of certainty: high.*
- ▶ *The incidence of infection following epidural steroid injection is rare, up to 1%–2%. Level of certainty: moderate.*
- ▶ *The incidence of SSI following lumbar spine surgery in patients receiving epidural steroid injection preoperatively may be increased if administered within 1 month prior to surgery, particularly for lumbar spinal fusion. Level of certainty: moderate.*
- ▶ *The incidence of SSI following cervical spine surgery in patients receiving epidural steroid injection preoperatively may be increased if administered within 6 months prior to surgery. Level of certainty: moderate.*
- ▶ *The incidence of discitis following discography overall ranges from 0% to 4.9% (likely increasing with multilevel disc access). Level of certainty: moderate.*
- ▶ *The incidence of discitis following cervical discography is 0.15%. Level of certainty: moderate.*
- ▶ *Utilization of a double-needle technique decreases the risk of infection compared with a single-needle technique for disc entry procedures. Level of certainty: low.*
- ▶ *The use of a stylet needle decreases the risk of infection during intradiscal procedures compared with non-stylet needles. Level of certainty: moderate.*
- ▶ *Infection following vertebral augmentation is rare, ranging from 0.35% to 2%. Level of certainty: moderate.*
- ▶ *The historical rate of infection following SCS device implantation ranges from 2.5% to 10% with results from a large US database demonstrating a 12-month device-related infection rate of 3%. Level of certainty: moderate.*
- ▶ *The rate of infection following intrathecal drug-delivery system implantation ranges from 2.5% to 9%. Level of certainty: moderate.*

### Consensus recommendations based on procedure type

- ▶ *Avoid IACS injection within 1 month of planned surgery for that joint. Evidence: grade D.*
- ▶ *Discuss with the surgeon the risks/benefits when considering IACS injection in a joint planned for replacement surgery within 3 months. Evidence: grade C.*
- ▶ *IACS injection to the knee should not be offered following TKA. Evidence: grade D.*
- ▶ *Candidates for facet joint procedures should be carefully assessed for risk factors associated with increased risk of infection. Evidence: grade C.*
- ▶ *Discography may be offered to select patients after careful assessment of risk factors, attempting to limit the total number of discs accessed per patient. Evidence: grade C.*
- ▶ *Use of a stylet needle is recommended when performing intradiscal procedures. Evidence: grade B.*

- A double-needle technique for performing intradiscal procedures is recommended. Evidence: grade B.

## INFECTIOUS COMPLICATIONS IN REGIONAL ANESTHESIA

Infectious complications broadly include insertion-site inflammation, localized abscesses, systemic infection, necrotizing fasciitis, or the devastating complication of CNS infections. Serious infectious complications following regional anesthesia are rare events, in that the probability of an event occurring in a small sample of patients typically employed in a clinical trial is low to none.<sup>151 152</sup> Clinical trials and databases may not provide information on the factors linked to these rare events. Therefore, it is crucial to study the occurrence, causes, contributory factors, clinical features, diagnosis, and management in case reports or series.

### Catheter/Insertion-site colonization

Measuring colonization in central neuraxial block catheters has used lower colony counts ( $\geq 1$  colony-forming unit [CFU]) to define colonization, however, colonization is often defined using the same criteria to determine central venous catheter (CVC) colonization, with a reference cut-off of  $\geq 15$  CFU using semi-quantitative methods (where the microorganisms are detected on the surface of the catheter) or  $\geq 100$  CFU using quantitative methods (where microorganisms are detected both inside and outside of the catheter), as these are known to be associated with CVC-related clinical infection. A similar association between defining colonization based on colony counts and infectious sequelae is not true for catheters used in regional anesthesia.<sup>153</sup> A higher CFU threshold has been used to define colonization in a study of PNBs, where a quantitative culture of the catheter tip needed to show at least one microorganism at a concentration of 1000 CFU/mL or greater.<sup>37</sup>

Numerous studies evaluated the incidence of catheter-tip colonization with epidural and intrathecal catheters<sup>37-44 153-164</sup> and one additional study explored the pattern of bacterial colonization. Epidural and intrathecal catheter colonization rate is noted to be in the range of 4.2%–29%, while a sole study on intrathecal catheters used for anesthesia estimated it to be approximately 7.2%.<sup>155</sup> Catheter colonization is influenced by a variety of factors such as the duration of catheter use, patient-risk factors for infection, tunneled catheters versus non-tunneled catheters, method of maintenance, the method of detection (semiquantitative vs quantitative methods), the site of sampling (skin entry site vs catheter shaft vs catheter tip), and the method of disinfection prior to catheter removal (as the catheter tip may be falsely contaminated if it comes in contact with the skin commensal organisms during removal).

Tunneled spinal catheters are occasionally placed for prolonged pain control in clinical settings when long-term analgesia is required.<sup>164</sup> Tunneled catheters may exit percutaneously to an external port or may be totally implanted with a subcutaneous port. Limited infection control data exist for tunneled catheters for pain control in the acute perioperative setting.<sup>157 164 165</sup>

A recent large retrospective study examined 22 411 adult patients receiving perioperative continuous thoracic epidural analgesia between 2007 and 2014. There were 12 870 patients who received tunneled epidural catheters and 9541 patients whose catheters were not tunneled. Tunneling was strongly associated with fewer catheter-related infections, even after adjustment for potential confounders.<sup>166</sup> Tunneled catheters have been used in chronic pain applications, initially predominantly for managing chronic cancer-related pain,<sup>167 168</sup> but later also

in treating chronic non-cancer pain.<sup>169 170</sup> Despite advantages of tunneling, percutaneously tunneled epidural catheters are limited by mechanical problems and infections. A retrospective study examined long-term administration of continuous analgesia through tunneled epidural catheters in 218 chronic non-cancer pain patients over a 5-year period. Of the 260 tunneled epidural catheters placed during that period, 15% were accidentally dislodged, 10% were discontinued due to mechanical malfunction, 18% removed due to patient preferences or ineffective pain relief, and 22% removed due to infection or suspicion of early infection.<sup>169</sup> Symptomatic infections in the epidural space occurred in 23 patients with complex regional pain syndrome. Tunneled epidural catheters were also discontinued in an additional 34 patients with superficial skin infections at the catheter entry site. The duration of catheter placement was not an independent risk factor for developing an infection, although the probability of remaining infection-free decreased with time.<sup>169</sup> An earlier retrospective study compared percutaneously tunneled catheters with an external port with those implanted with subcutaneous ports in patients with cancer-related pain.<sup>171</sup> There were 52 tunneled catheters with subcutaneous ports, 41 tunneled catheters without subcutaneous ports, and 157 epidural catheters that were not tunneled. Unlike the other catheters, there were no dislodgments of tunneled catheters with implanted subcutaneous ports. Additionally, the infection rate per 1000 catheter days in the group of patients with subcutaneous ports was half that of patients with percutaneous catheters; and no infections were noted at ports before day 70 postimplant compared with infections as early as 1 week in the percutaneous group.<sup>171</sup>

Analogous to the epidural route, tunneled intrathecal catheters have been used in both cancer and non-cancer pain,<sup>172-174</sup> with reportedly higher efficacy of pain relief and fewer adverse events with tunneled intrathecal catheters compared with tunneled epidural catheters.<sup>172</sup> A prospective non-randomized cohort study by Nitescu *et al* examined complications of externalized tunneled intrathecal catheters in 200 patients with cancer-related pain.<sup>174</sup> The authors describe the use of Millipore filters in the infusion line and steel sutures to secure the catheters to the skin.<sup>175</sup> The treatment duration was up to 575 days with a median of 33 days. Only two infections occurred: a local catheter entry site abscess in one patient and a case of meningitis in another patient. Both received antibiotics and had the catheters replaced with resumption of intrathecal therapy for several weeks afterwards.<sup>174</sup> Two local infections occurring at the catheter entry sites were reported in a retrospective study of 51 patients with cancer-related pain receiving intrathecal analgesia.<sup>176</sup> In a prospective study on ziconotide using tunneled intrathecal catheters, four of the first 40 patients developed meningitis between the second and third weeks of infusion. This led to updating the protocol to restrict the titration phase to 1–2 weeks. Among the 64 patients who experienced adverse effects, no cases of meningitis occurred during the initial 2-week titration period.<sup>177</sup>

### Insertion-site infection

Although catheters often become colonized after insertion, infections at the insertion site or in the surrounding soft tissue are rare. Additionally, there is no demonstrated correlation between the rate of colonization and the incidence of inflammation or infection at the insertion site. Catheter-related infection was defined in one study as the ‘isolation of the same microorganism from the colonized catheter and from at least one

blood culture and/or a culture from an abscess with absence of any other infectious focus.<sup>37</sup> This is similar to the definition for catheter-related bloodstream infection, which requires the isolation of the same organism from the peripheral blood as from the catheter tip,<sup>150 178</sup> but it is seldom possible to establish in clinical practice as catheter-tip or blood cultures are not routinely obtained.<sup>179 180</sup> The development of insertion-site inflammation was significantly associated with catheter duration (>4 days)<sup>157</sup> and in one study, a 40% increase in risk of infection was noted for each additional postoperative day of keeping epidural catheters in situ.<sup>158</sup> A similar temporal association is noted with PNB catheters as well.<sup>166</sup> An increased risk of insertion-site infection has also been noted with thoracic and general abdominal surgeries<sup>158</sup> and in patients with thoracic or abdominal trauma,<sup>39</sup> but better evidence is needed to determine if surgical site or insertion site influences catheter-colonization rates.

One study looked at both catheter-site infection and inflammation and noted that the occurrence of catheter-site inflammation is more common than catheter-site infections (5.3% vs 0.5%).<sup>157</sup> However, it has been noted that not all patients with bacteremia and/or microorganisms present on the catheter have signs and symptoms of infection.<sup>159 160</sup> Furthermore, the incidence of infection relies on the factors pertinent to colonization, and additionally on the source of the data (prospective vs retrospective). Prospective studies tend to report a higher incidence compared with retrospective studies. The incidence of infections involving central neuraxial blocks, in general, is noted to be anywhere from 1 per 100 000 to as high as 4% of cases,<sup>45 62 181–185</sup> but is more common with epidural catheters (ranging from 0.07 per 100 000 to 10%) compared with spinal anesthesia (0.01–40 per 100 000).<sup>47 183 186 187 188 189 190 191 192 193 194 195 196 197–199</sup>

Peripheral catheter infections can arise from bloodstream spread, drug infusion contamination, or pathogens entering through the catheter site, with the latter being the primary cause of most catheter-related infections.<sup>200 201</sup> Certain risk factors are also relevant: admission to intensive care, absence of perioperative antibiotics, male sex, femoral, axillary, and interscalene regions.<sup>201–203</sup> Duration of catheter retention has also been correlated with chance of infection increasing over time with catheter use after 2–4 days.<sup>166 203 204</sup>

A large multicenter study including 24 103 peripheral nerve catheters, placed via either nerve stimulator or ultrasound guidance under strict aseptic technique, found an incidence of infection of 2.9%.<sup>166</sup> This study included a maximum catheter duration of 15 days, which may have contributed to this high incidence.

### CNS infections: incidence

The incidence of CNS infection following central neuraxial block is rare across a variety of sample sizes and patient populations,<sup>45 62 181 184 205</sup> in the range of 1–4.9 per 100 000 (95% CI 7 to 13 per million).<sup>182 183 185</sup> Similar to overall infectious episodes, spinal procedures are associated with low risk of CNS infections. Pitkänen *et al*<sup>183</sup> estimated the incidence of CNS complications to be approximately 8.3 per million spinal anesthetic procedures and approximately 11.3 per million epidural procedures, and a similar finding was noted recently by Makito *et al*.<sup>182</sup>

The details of individual case reports of infectious complications following epidurals<sup>46 49</sup> and spinals<sup>58–61</sup> are consistent with the findings seen in prospective and retrospective studies on infectious complications of regional anesthesia. The infectious complications of neuraxial blocks are limited to superficial or

CNS infections (organ/space infections with PNB) and can lead to severe systemic or deep infections such as psoas abscesses,<sup>206–208</sup> pyogenic spondylitis,<sup>209 210</sup> discitis,<sup>211</sup> necrotizing fasciitis,<sup>212 213</sup> vertebral osteomyelitis,<sup>214</sup> cerebrospinal fluid (CSF) cutaneous fistula,<sup>215 216</sup> disseminated infection,<sup>217</sup> sepsis, and death.<sup>218</sup> Patients with sensorimotor deficits or those whose time from neuraxial anesthesia to diagnosis of CNS infection was longer were more likely to have serious sequelae or death compared with those with a shorter time to diagnosis or a milder clinical presentation. A database study by Rosero and Joshi<sup>185</sup> noted no increase in the incidence of infectious complications following central neuraxial blocks, yet a recent systematic review and meta-analysis by Zorrilla-Vaca *et al*<sup>54</sup> showed a linear increase in the incidence of meningitis following central neuraxial blocks. Whether a similar trend exists for epidural-related infections is currently unknown.

### Peripheral nerve blocks

Infections after ultrasound-guided continuous PNBs are rare but can be significant.<sup>219 220</sup> Studies report low to no infection rates, with one study using single-injection PNBs detailing zero infections in 7476 patients,<sup>221</sup> and another with no significant infections among 211 femoral nerve catheter placements, although the rate of bacterial colonization at the catheter site in the latter study was 57%.<sup>222</sup> A retrospective review of 9649 patients receiving continuous posterior lumbar plexus blockade also reported zero infections.<sup>223</sup> However, infections and severe complications have occasionally occurred, particularly when aseptic protocols are not strictly adhered to.<sup>200</sup>

Catheter colonization is relatively common, varying between 6% and 46% in studies.<sup>163 203 204 222–228</sup> A prospective study of 747 cases found a low incidence of colonization (10%) and infection (0.1%) when strict sterile techniques (sterile probe and cable coverings) were used.<sup>37</sup>

The primary consistent risk factor influencing colonization rates is catheter use beyond 48 hours<sup>37 201 203</sup>; there is equivocal evidence for other factors, including immunocompromised status,<sup>37 181 229</sup> antibiotic therapy prior to insertion of PNB catheters (protective effect),<sup>37</sup> absence of antibiotic prophylaxis,<sup>181 204 224 225</sup> need for intensive care unit (ICU) stay,<sup>204</sup> type of needle (a Tuohy needle had a higher colonization rate compared with a short bevel needle),<sup>225</sup> body habitus,<sup>230</sup> location of block (PNB catheters in the neck and groin seem to have a higher colonization rates),<sup>163 203 228</sup> or higher ASA class.<sup>181</sup> Severe infections often require antibiotics or even surgical intervention.

The most common organisms colonizing PNB catheters are the CoNS, mainly *S. epidermidis*. The most common cause of infectious complications is *S. aureus*, similar to that seen with epidural procedures. Positive cultures from catheter tips may not always indicate infections, as contamination can occur during catheter removal. The infection rate is low, and only a small proportion of positive catheter cultures are likely to represent true infections (0%–3.2%).<sup>203 222 231–233</sup> Erythema and inflammation found at the catheter site are sometimes due to mechanical irritation not infection.<sup>203</sup>

While the diagnosis of infectious complications following PNB is primarily based on clinical features, it is not uncommon to use imaging modalities such as ultrasonography or CT scan in the evaluation of infections.<sup>37 204</sup> Case reports of infectious complications following PNB<sup>46 58 219 220 234–247</sup> are consistent with the other published evidence in that the prognosis tended towards full recovery with medical or surgical management, except in those cases with necrotizing fasciitis.

## Statements

- ▶ Catheter colonization is common and is directly related to the duration of catheterization, and a greater incidence of colonization may be seen with the use of catheters beyond 4 days. Level of certainty: moderate.
- ▶ PNBs have a greater incidence of catheter colonization compared with central neuraxial catheters. Level of certainty: moderate.
- ▶ The reported incidence of infection associated with percutaneous tunneled neuraxial catheters is approximately 10%. Level of certainty: moderate.
- ▶ With indwelling catheters, the probability of remaining infection-free decreases with time. Level of certainty: moderate.
- ▶ Implanting a subcutaneous port for neuraxial catheters decreases the risk of infection compared with percutaneous neuraxial catheters. Level of certainty: moderate.
- ▶ Spinal anesthesia is associated with fewer infectious complications compared with epidural anesthetic techniques. Level of certainty: moderate.
- ▶ Infections may occur with tunneled neuraxial catheters with likely lower rates in intrathecal compared with epidural catheters. Level of certainty: moderate.
- ▶ The duration of infusion may not be a determinant of the risk for infection, although the probability of remaining infection-free decreases with time. The risk of meningitis appears to be higher after the first 2 weeks of infusion with externalized (not internalized or tunneled) intrathecal catheters. Level of certainty: moderate.

## Recommendations

- ▶ Consider limiting the duration of infusion in a percutaneous tunneled catheter and placing a subcutaneous port to minimize the risk of infection. Evidence: grade B.
- ▶ Prolonged use of regional nerve block catheters may increase the risk of infection. Extended use beyond 4–5 postprocedure days should be decided on the risk-to-benefit profile of continuing such therapies while carefully monitoring for any signs and symptoms of infection. Evidence: grade C.
- ▶ If using an externalized neuraxial catheter, prolonged use beyond 2 weeks should be avoided when possible to reduce the risk of meningitis. Evidence: grade B.

## THE ROLE OF THE ANESTHESIOLOGIST IN PERIOPERATIVE INFECTION RISK-REDUCTION STRATEGIES

Anesthesiologists play a crucial role in reducing perioperative risks through strict adherence to aseptic techniques during regional anesthesia and interventional pain medicine procedures, which includes intravenous sedation/analgesia and catheter insertion for local anesthesia.<sup>203</sup> Over the past decade, research has led to infection control guidelines for anesthesiologists intended to prevent the transmission of pathogens in the anesthesia work area (AWA) and when performing regional and neuraxial procedures.<sup>248 249</sup>

Bacterial contamination of the AWA occurs in as early as 4 min and increases significantly during the process of patient care.<sup>250 251</sup> This contamination, notably of injection ports by common pathogens (eg, *Enterococcus*, *S. aureus*, *Klebsiella*, *Acinetobacter*, *Pseudomonas*, and *Enterobacter* spp organisms), has been directly linked to higher patient mortality and healthcare-associated infections (HAIs).<sup>251</sup> Such pathogens are more likely to harbor more pathogenic strain characteristics (eg, increased desiccation tolerance, *S. aureus* sequence type 5) that

make infections more difficult to treat when they develop.<sup>252–256</sup> Factors contributing to injection port contamination include contamination of provider hands,<sup>257–260</sup> patient skin,<sup>261</sup> and the environment (adjustable pressure-limiting valve and agent dial of the anesthesia machine).<sup>250 251 261</sup> Evidence from genetic analyses ties AWA pathogens to a substantial percentage of postoperative HAIs, highlighting the need for better infection control practices across all anesthesia modalities to enhance perioperative patient safety.<sup>251 255</sup>

A multifaceted approach is required to address the complex interplay of contributing reservoirs.<sup>250–255 260–263</sup> Improvement measures should address the following: (1) hand hygiene, (2) routine and between-case environmental cleaning, (3) preoperative patient decolonization, and (4) injection port/syringe tip disinfection, and monitoring.<sup>248 249 255</sup>

### Environmental cleaning

Environmental contamination exceeding 100 colonies per surface sampled is a potent transmission vehicle associated with increased risk of injection port contamination, which, in turn, is associated with increased patient morbidity and mortality.<sup>250</sup> Improved frequency and quality of cleaning of the AWA following induction of anesthesia and patient stabilization via use of surface disinfection wipes can reduce the proportion of high-touch surfaces in the AWA that reach this level of contamination.<sup>257–259 264</sup> Using double gloves with the outer pair removed and discarded after verified intubation can reduce environmental contamination.<sup>257</sup>

### Syringe tip and injection port disinfection

Bacterial contamination of syringes can occur after a single use,<sup>265</sup> and routine medication handling in the AWA can lead to injection of bacterial pathogens such as *S. aureus* directly into the patient's bloodstream via intravenous catheter injection ports or indirectly into the bloodstream or epidural space via contamination of medication vials.<sup>266–268</sup> Propofol contamination has been directly linked to development of postoperative sepsis.<sup>268–270</sup> Improved syringe tip and injection port disinfection in the AWA has been shown in an RCT involving over 500 patients to reduce both injection port contamination and 30-day HAIs.<sup>271</sup>

### Host optimization strategies

Maintaining normothermia (at least a 36°C core temperature) on arrival to the postanesthesia care unit (PACU)<sup>272</sup> and optimizing glycemic control (140–180 mg/dL)<sup>273</sup> may lower postoperative infection rates.<sup>274 275</sup> Stulberg *et al* found that adherence to such surgical infection prevention measures was associated with a significantly lower risk of postoperative infection.<sup>274</sup> High concentration of supplemental oxygen has been shown in well-designed randomized trials to reduce the incidence of SSIs.<sup>276</sup>

### Proactive infection mitigation strategies

Anesthesia providers are well positioned to improve perioperative patient safety by reducing bacterial transmission and associated infection risk. An RCT demonstrated significant reduction in *S. aureus* transmission and 60-day SSIs through a comprehensive approach that includes better hand hygiene,<sup>277</sup> postinduction environmental cleaning with surface disinfection,<sup>264 278</sup> targeted ultraviolet-C treatment for operating rooms with high-risk *S. aureus* strains,<sup>255</sup> organization of spaces into clean and dirty areas,<sup>264</sup> preoperative patient decolonization using 5% povidone iodine<sup>263 278</sup>

and 4% chlorhexidine gluconate wipes,<sup>278</sup> and disinfection of syringe tips and injection ports with isopropyl alcohol-impregnated caps.<sup>271 278 279</sup>

### Statements

- *Perioperative adherence to evidence-based infection control measures reduces the incidence of SSIs. Level of certainty: high.*
- *Maintaining perioperative normothermia (core temperature of 36°C on arrival to the PACU) can reduce SSIs. Level of certainty: moderate.*
- *Optimizing perioperative glucose control can reduce SSIs. Level of certainty: moderate.*

### Recommendations

- *Syringe tip disinfection should be practiced by anesthesia team members in every case. Evidence: grade A.*
- *Frequent hand hygiene as part of a multimodal approach to limit infection risk is recommended. Hand hygiene should be performed: (1) before aseptic tasks (eg, epidural injections, PNBs); (2) on entering and exiting the OR; (3) prior to handling the anesthesia cart and associated contents; (4) after removing gloves; and (5) when hands become contaminated or soiled. Evidence: grade A.*
- *Perioperative patient normothermia should be maintained. Evidence: grade B.*
- *Blood glucose control should be optimized perioperatively. There is evidence suggesting lower risk of SSIs in patients with perioperative blood glucose  $\leq 150$  mg/dL. Evidence: grade B.*

## PATIENT RISK FACTORS AND RISK REDUCTION OPTIMIZATION

### Patient risk assessment

General preprocedural assessment of risk factors for infection is guided by good clinical judgment and should include review of the patient's history, including any recent infections, current or recent antibiotic use, or symptoms suggesting infection.<sup>150</sup> On the day of the procedure, the patient should be assessed for active symptoms of infection or conditions that might warrant postponing the procedure, such as fever, cough, shortness of breath, diarrhea, skin and soft tissue infection. Indwelling device sites should be checked for signs of infection. Laboratory and diagnostic testing should be based on preprocedural history and physical examination.

When considering general patient risk factors for infection following regional and interventional pain medicine procedures, there are no RCTs to guide management. Most information stems from large observational studies, case series, and case reports.<sup>102 200 280</sup> ICU admission is a known independent risk factor for peripheral nerve catheter infections,<sup>200</sup> but there are no data demonstrating overall illness severity or revision surgery as a risk factor for infection related to peripheral or neuraxial blockade. Smoking is a known risk factor for SSIs,<sup>281</sup> but its effect on pain procedure infection risks is unclear. In a retrospective, multicenter review of over 2700 patients, Hoelzer *et al* found no link between revision surgery and tobacco use and increased infection rates following SCS implantation.<sup>147</sup> While long-term corticosteroids and other immunosuppressants increase the risk of infection in general, there is no evidence they increase the risk of infections from pain procedures. A Cochrane review found no evidence that the use of perineural or intravenous dexamethasone increases the risk of infection associated with PNB.<sup>282</sup>

### Nutritional status

A patient's nutritional status could also influence the likelihood of infection after a procedure. Protein-calorie malnutrition impairs host immunity with detrimental effects on the T-cell system, resulting in increased opportunistic infection.<sup>283</sup> There are no data on the risk of infection due to malnutrition specific to acute and chronic pain procedures. Malnutrition has been significantly associated with poorer outcomes, including increased infectious complications and increased hospital length of stay, in surgical patients with cancer<sup>284 285</sup> and with lumbar fusion.<sup>286</sup> Decreased preoperative serum albumin, a surrogate marker of nutritional status, has been correlated with increased risk of postoperative infection in orthopedic<sup>287 288</sup> and cardiac surgery.<sup>289</sup> Vitamin D deficiency has also been noted to be a risk factor for infection in the first 6 months after liver transplant and for bacterial infections occurring 6–30 months post-transplant.<sup>290</sup> The American College of Surgeons National Surgical Quality Improvement Project study of 5441 patients who underwent posterior cervical spine surgery found BMI  $>35$  to be associated with increased risk of SSI (OR 1.78,  $p=0.003$ ).<sup>291</sup> Higher BMI and lower preoperative WBC count have also been noted as independent predictors of deep infection after allograft reconstruction of the proximal tibia.<sup>292</sup>

Limited evidence suggests that arginine supplementation may boost immune function in surgical patients by enhancing T-lymphocyte response and T-helper cell numbers, potentially reducing infection risks in high-risk surgical populations.<sup>283</sup>

### Statement

- *General patient risk factors for increased infection in the procedural setting include ICU hospitalization, tobacco use, concurrent use of immunosuppressant medications, malnutrition (including low preoperative albumin), and obesity. Level of certainty: moderate.*

### Recommendation

- *Identify and optimize patient risk factors (eg, tobacco use, diabetes mellitus) prior to implantable device therapy surgeries. Evidence: grade B.*

### Specific medical comorbidities

Few RCTs exist to inform decision-making for patients' conditions that increase the risk of infection during pain management procedures. In SCS patients, Hoelzer *et al* in a retrospective study found no additive infection risk associated with diabetes mellitus or obesity.<sup>147</sup> However, patients with hemoglobin A1c levels of  $\geq 7.5$  mg/dL within 3 months of lumbar decompression had a higher risk of infection (OR 2.9, 95% CI 1.8 to 4.9).<sup>293</sup> Postoperative hyperglycemia increases the risk of SSI.<sup>200</sup>

Patients with HIV whose CD4 counts are  $<200$  cells/mm<sup>3</sup> experience higher postsurgery mortality and infections than those with higher counts and those unaffected with HIV, although data on HIV's impact on infection risk in pain procedures are limited.<sup>294</sup> One study reported seven cases of meningitis (among 112 patients with AIDS or cancer), who were administered intrathecal ziconotide or placebo via externalized (not internalized or tunneled) catheters, but the authors did not distinguish between patients with AIDS and cancer in their reporting.<sup>295</sup>

Cancer and chemotherapy elevate infection risks in pain procedures. A systematic review found a 1.4% deep infection rate, 2.3% superficial infection rate, and 2.9% overall catheter-related infection rate in the treatment of cancer-related pain using externalized catheters.<sup>296</sup> The authors were unable to identify

specific risk factors that may predispose to infection. Infection rates following IDD systems for cancer pain remain low but vary, with one study reporting a 0.9% infection rate<sup>297</sup> and another a 3.2% risk of infection requiring surgical intervention.<sup>298</sup>

Minimizing postoperative infections involves optimizing the innate immune response through nutritional support, medication management, and minimizing surgical trauma.<sup>299</sup> Promising strategies include supplemental oxygen, maintenance of core body temperature, managing blood glucose, and *S. aureus* decolonization.<sup>300</sup>

### ***S. aureus* colonization: identification and management strategies**

The incidence of MRSA infection after a major surgical procedure is estimated to be 1%.<sup>31 33 301</sup> Notably, both MSSA and MRSA colonization are correlated with a twofold to ninefold increased risk of SSIs.<sup>150</sup> Infections following ESIs are mostly attributed to inadequate infection-control practices rather than patient factors.<sup>115</sup> There is no evidence that MRSA or MSSA colonization are infection risks for regional anesthetic or chronic pain injections that do not involve implanted devices. Approximately two-thirds of implantable device infections are caused by *S. aureus* or CoNS.<sup>36</sup> Microbial biofilm can result in more severe infection and additional surgical revisions due to SSI.<sup>302</sup> Staphylococci are recognized as the most frequent causes of biofilm-associated infections.<sup>303</sup>

Patients undergoing pain procedures may be colonized with *S. aureus*. A recent study examining 232 SCS surgical patients demonstrated that 23.3% (n=54/232, 95% CI 18.0% to 28.6%) of patients were preoperatively colonized by *S. aureus* with the following classification: 4.3% (n=10/232, 95% CI 2.1% to 7.8%) were positive for MRSA and 20.2% (n=46/228, 95% CI 15.2% to 26.0%) for MSSA.<sup>35</sup> Furthermore, the study emphasized the importance of testing for both MSSA and MRSA since MRSA screening alone would not have identified >90% of *S. aureus*-colonized patients.<sup>35</sup> MRSA/MSSA testing and decolonization have been suggested for colonized patients prior to pain device implantation.<sup>304</sup>

Randomized trials indicate that mupirocin-chlorhexidine treatment reduces SSIs among *S. aureus* carriers compared with placebo.<sup>263 305 306</sup> Swabbing of the nares is the most sensitive method for detecting MRSA/MSSA.<sup>307 308</sup> Decolonization studies have shown continued eradication from 10 days to 3 months.<sup>308 309</sup> However, despite decolonization, some patients remain colonized,<sup>310</sup> especially those with MRSA, throat colonization, or age >80 years.<sup>311</sup> Alternative decolonization methods, such as povidone iodine, have not shown the same effectiveness as chlorhexidine-based protocols.<sup>312</sup>

Multiple prospective observational studies examined use of mupirocin for 5 days prior to surgery with and without chlorhexidine in patients colonized with MRSA/MSSA and showed mupirocin to be effective at decolonizing<sup>313–315</sup> and/or preventing SSIs.<sup>306 316–327</sup> However, in one observational study of thoracotomy for lung resection, the rates of SSI were not significant with this protocol.<sup>328</sup> The data are limited for chlorhexidine alone. Kapadia *et al* conducted a prospective cross-comparison study that showed a reduction of SSIs in all patients who used chlorhexidine wipes, regardless of carrier status.<sup>329</sup>

#### **Statements**

- *S. aureus* colonization may be present in patients undergoing implantable neuromodulation procedures. Level of certainty: moderate.

- Patients colonized with nasal MRSA preoperatively have a higher incidence of MRSA SSIs compared with those who are not colonized with nasal MRSA. Level of certainty: moderate.
- *S. aureus* decolonization lasts for 10–90 days in most patients. Level of certainty: moderate.
- Prophylactic intranasal application of mupirocin in individuals not colonized with MRSA/MSSA does not notably reduce the rate of *S. aureus* SSIs. Level of certainty: high.
- Chlorhexidine-based products have been shown to be superior to povidone iodine-based products in reducing skin flora and SSI rates when used as a preoperative skin preparation. Level of certainty: high.

#### **Recommendations**

- Patients should be tested for *S. aureus*, including MRSA and MSSA, using a nasal swab, and decolonization should be performed in colonized patients prior to pain device implantation. Evidence: grade B.
- When performing decolonization, use mupirocin nasal application and chlorhexidine body scrubs for 5 days in patients screening positive for MSSA or MRSA to reduce SSI. The decolonization should occur no earlier than 10 days prior to the planned surgery. Evidence: grade B.
- In individuals known previously to be MSSA or MRSA carriers, decolonization should be repeated prior to additional procedures beyond 10 days from initial decolonization for implantable pain procedures. Evidence: grade C.

#### **Dermatological conditions and the increased risk of SSI**

While no studies directly involving neuromodulation and dermatological conditions have been conducted, there can be several extrapolations made from the literature of related disciplines. A study by Kawata *et al* on 30536 patients undergoing anterior cruciate ligament reconstruction found a higher SSI rate among those with atopic dermatitis, marking it as an independent SSI risk factor.<sup>330</sup> Another study by Fukunaga *et al* observed MRSA mediastinitis in patients with atopic dermatitis after cardiac surgery, indicating a specific risk for those undergoing median sternotomy.<sup>331</sup> A review of 38 patients with psoriasis undergoing hip arthroplasties without prophylactic antibiotics therapy noted a 9.1% overall infection rate,<sup>332</sup> suggesting a higher risk. A study of patients with psoriasis vulgaris undergoing knee arthroplasties indicated a low rate of deep infections, implying that psoriasis did not elevate the risk of SSIs.<sup>333</sup> These findings, although not specific to neuromodulation, highlight the potential relevance of certain skin conditions in increasing infection risks in pain medicine implantable device surgeries.

#### **Statement**

- Psoriasis and atopic dermatitis may increase the risk of SSI. Level of certainty: low.

#### **Immunosuppressive agents, SSIs, and risk-modification strategies**

Immunosuppressive drugs, critical for treating autoimmune disorders like systemic lupus erythematosus (SLE) and rheumatoid arthritis, significantly impact infection risk. The CDC considers a prednisone dose of >20 mg/day for at least 2 weeks to be the threshold for increased risk of infection following attenuated live vaccine administration.<sup>334</sup> Studies link chronic preoperative corticosteroid use to higher postsurgical infection risks in lumbar surgery<sup>335 336</sup> and joint arthroplasty,<sup>337 338</sup> although findings vary, with some research not showing a significant link

to SSIs but rather to urinary-related<sup>336</sup> or sepsis-related complications.<sup>336 338</sup> The timing of IACS relative to TKA is crucial; injections within 2–4 weeks or 3 months<sup>79</sup> before TKA increase infection risks, with no added risk if surgery occurs 3 or more months after an IACS.<sup>82</sup>

Disease-modifying antirheumatic drugs (DMARDs) are used in the treatment of inflammatory arthritides, connective tissue disorders, and other autoimmune conditions such as SLE, multiple sclerosis, and inflammatory bowel disease. These drugs are classified as conventional synthetic compounds (eg, methotrexate, hydroxychloroquine, sulfasalazine, leflunomide, doxycycline) or biologic agents (tumor necrosis factor [TNF] inhibitors, eg, adalimumab, etanercept, infliximab, rituximab, secukinumab, tocilizumab, tofacitinib), or targeted synthetic DMARDs (eg, the recently introduced Janus kinase [JAK] inhibitors [facitinitib, baricitinib, and upadacitinib]).<sup>339 340</sup> These medications also affect infection risk, underlining the need for careful management in the perioperative period.

The complexity of these drugs and frequent introduction of new DMARDs led national organizations to develop guidelines in the prescription and monitoring of these drugs, although detailed recommendations are not covered here.<sup>340–344</sup> Biologic DMARDs typically increase the risk of infection after surgery, especially when multiple immunomodulatory drugs are used.<sup>341 345–353</sup> For this reason, rheumatology organizations, some in conjunction with surgeons and infectious disease specialists, issued practice recommendations on the discontinuation of these agents prior to surgery.<sup>339 341 350 354</sup> In view of the paucity of RCTs resulting in low-quality or moderate-quality evidence, the recommendations are conditional. A conditional recommendation implies that most individuals would want the recommended course of action but many would not, thus individual choices vary depending on preferences and values.<sup>339</sup>

The American College of Rheumatology/American Association of Hip and Knee Surgeons (ACR/AAHKS) guideline and the National Health and Medical Research Council-endorsed Australian Living Guideline for the Pharmacologic Management of Inflammatory Arthritis are current.<sup>339 350 354</sup> The ACR/AAHKS recommendations include the continuation of conventional synthetic DMARDs, supported by studies showing the absence of increased infection risk and mild flare-up when these drugs are paused before surgery. They recommended that biologic and targeted synthetic DMARDs be stopped and the surgery be planned when the next dose is due<sup>350 354</sup> (table 5).

The Australian National Health and Medical Research Council position paper also conditionally recommends against the routine discontinuation of conventional synthetic DMARDs in the perioperative period, except for methotrexate and leflunomide, based on RCTs in patients with rheumatoid arthritis (table 5). They also advise a cautious approach to stopping biologic DMARDs, based on observational studies (table 5). The guidelines recommend pausing newly introduced targeted DMARDs, based on the lack of publication on these drugs,<sup>339</sup> with a longer break for JAK inhibitors due to the increased risk of venous thrombosis, a consideration not mentioned by the ACR/AAHKS.

Surgery at the end of a dose interval means that the drug levels are low. The drug is to be resumed when the wound is healed and in the absence of infection.

Our practice guideline prefers the simpler and more clinically adaptable ACR/AAHKS recommendations for DMARD management (table 6), although the Australian recommendations, particularly for rituximab, are valid alternatives. Clinicians are advised to regularly check for updates on these guidelines based on new research findings.

Currently, there are no specific practice recommendations for managing patients on DMARDs undergoing PNBs, intra-articular, or neuraxial procedures/implants. There are two reports of infection after neuraxial injections in patients on DMARDs and both were taking prednisone.<sup>355 356</sup>

Our recommendations balance the necessity of these medications against the minor adverse events when the drugs are stopped, the consequences of infection (neuraxial, deep vs superficial), and the absence of studies to guide us. Similar to the ACR and Australian guidelines, our recommendations are conditional, and decisions should involve the pain medicine and managing physicians and the patient.

#### Statement

- *Patients taking DMARDs, with or without corticosteroid, should be considered immunocompromised and at increased risk of procedure-related infections. Level of certainty: low.*

#### Recommendations for patients on DMARDs

- *Superficial PNB: the DMARDs, including the biologic drugs and targeted DMARDs may be continued when a superficial PNB is performed. Evidence: grade I (insufficient).*

**Table 5** Recommendations of the American College of Rheumatology/American Association of Hip and Knee Surgeons (ACR/AAHKS) guideline and the Australian National Health and Medical Research Council position paper for patients on DMARDs undergoing surgery

DMARDs	ACR/AAHKS guideline	Australian National Health and Medical Research Council position paper
Conventional synthetic csDMARDs*	Continue	Continue except methotrexate and leflunomide
		Methotrexate, withhold one dosing cycle prior to surgery
		Leflunomide, stop approximately 7 days before surgery
bDMARDs†	Withhold, duration based on dosing interval	Withhold one dosing cycle
	Rituximab: surgery on month 7 after stoppage	Rituximab (half-life 21 days): surgery 3 months after last dose
Targeted DMARDs‡	JAK inhibitors: withhold 3 days before surgery	bitors: stop approximately 7 days before surgery

\*csDMARDs: apremilast, doxycycline, hydrochloroquine, leflunomide, methotrexate, sulfasalazine.

†bDMARDs: abatacept, adalimumab, anakinra, certolizumab, etanercept, golimumab, IL-17 secukinumab, infliximab, ixekizumab, rituximab, tocilizumab, ustekinumab.

‡JAK inhibitors: baricitinib, tofacitinib, upadacitinib.

bDMARDs, biologic DMARDs; csDMARDs, conventional synthetic DMARDs; DMARDs, disease-modifying antirheumatic drugs; IL, interleukin; JAK, Janus kinase.

**Table 6** American College of Rheumatology/American Association of Hip and Knee Surgeons on the perioperative use of DMARDs\*

Conventional synthetic DMARDs (continue throughout surgery)	Recommended timing of surgery
Methotrexate	Anytime
Sulfasalazine	Anytime
Hydroxychloroquine	Anytime
Leflunomide (Arava)	Anytime
Doxycycline	Anytime
Apremilast (Otezla)	Anytime
Biologic DMARDs to withhold prior to surgery	
Infliximab (Remicade)	Week 5, 7, or 9 (every 4, 6, or 8 weeks treatment)
Adalimumab (Humira)	Week 3
Etanercept (Enbrel)	Week 2
Golimumab (Simponi)	Week 5 (every 4-week subcutaneous treatment); week 9 (every 8-week intravenous treatment)
Abatacept (Orencia)	Week 5 (intravenous treatment); week 2 (subcutaneous treatment)
Certolizumab (Cimzia)	Week 3 (intravenous treatment) or 5 (subcutaneous treatment)
Rituximab (Rituxan)	Month 7
Tocilizumab (Actemra)	Week 2 (subcutaneous treatment); week 5 (intravenous treatment)
Anakinra (Kineret)	Day 2
Secukinumab (Cosentyx)	Week 5
Ustekinumab (Stelara)	Week 13
Ixekizumab (Taltz)	Week 5
Guselkumab (Tremfya)	Week 9
Targeted DMARDs, JAK inhibitors	
Tofacitinib (Xeljanz)	Day 4
Baricitinib (Olumiant)	Day 4
Upadacitinib (Rinvoq)	Day 4

Specific recommendations for systemic lupus erythematosus not included.

Adapted from Goodman *et al.*<sup>354</sup>

\*NOTE: Biologic agents include the TNF inhibitors such as adalimumab, etanercept, infliximab, rituximab, secukinumab, tocilizumab, tofacitinib. Targeted synthetic DMARDs include the recently introduced JAK inhibitors tofacitinib, baricitinib, and upadacitinib. Conventional synthetic DMARDs (eg, methotrexate, hydroxychloroquine, sulfasalazine, leflunomide, doxycycline) can be continued, per ACR/AAHKS guidelines.

DMARDs, disease-modifying antirheumatic drugs; JAK, Janus kinase.

- *Deep PNB, whether or not a tunneled catheter is placed: stopping the biologic drug and/or targeted DMARDs should be considered. Evidence: grade I (insufficient).*

- *Visceral deep sympathetic block: stopping the biologic drug and/or targeted DMARDs should be considered. Evidence: grade I (insufficient).*
- *Intra-articular joint injection: stopping the biologic drug and/or targeted DMARDs should be considered. Evidence: grade I (insufficient).*
- *Neuraxial block, whether or not a tunneled catheter is placed: stopping the biologic drug and/or targeted DMARDs should be considered with a neuraxial corticosteroid injection (epidural, facet joint, SIJ). If a patient is taking conventional synthetic DMARDs with an oral corticosteroid, discontinuation of these drugs should also be considered. Evidence: grade C.*
- *Surgical interventional pain procedures (intrathecal pumps, SCS device implantation): stopping the biologic drug and/or targeted DMARDs should be considered with surgical interventional pain procedures. If a patient is taking conventional synthetic DMARDs with an oral corticosteroid, discontinuation of these drugs should be considered. Evidence: grade C.*

## PREPROCEDURAL RECOMMENDATIONS

### Preoperative antibiotic administration for pain therapy procedures

Preoperative antibiotic prophylaxis has been shown to significantly reduce the risk of SSIs, and the incidence of wound infection by approximately 50%, regardless of type of surgery.<sup>357</sup> Antibiotic prophylaxis (table 7) is recommended for implantable pain therapies (class D procedures), and class C procedures (classes are described in table 3). Proper antibiotic selection, route of administration, dosing, and timing are critical, as suboptimal implementation has been found to increase the risk of infection two-fold to six-fold.<sup>358–359</sup> Cephalosporins (eg, cefazolin) are recommended as first-line agents. If a patient has a  $\beta$ -lactam allergy, clindamycin is the preferred alternative. Vancomycin is only recommended if the patient is colonized with MRSA or at high risk for MRSA (eg, residents of institutions that have a high rate of MRSA infections).<sup>360–362</sup> In individuals with vancomycin allergy, daptomycin may be considered.<sup>363</sup>

For antibiotic prophylaxis to be effective, minimum inhibitory concentrations must be reached prior to surgical incision and maintained through the duration of the surgery. Therefore, weight-based dosing is critical. Preoperative antibiotics should be administered by the intravenous route prior to breaching the skin (30–60 min for cefazolin or clindamycin, 120 min for vancomycin). Redosing is needed when the duration of surgery is longer than two half-lives of the administered antibiotic (table 7). Considering the usual duration of interventional pain procedures, redosing standard preoperative antibiotics is generally

**Table 7** Prophylactic antibiotic recommendations\*

Antibiotic	Standard intravenous dosing	Timing prior to incision	Half-life†	Redosing interval†	Indications
Cefazolin	1 g $\leq$ 60 kg; 2 g >60 to 120 kg; 3 g >120 kg	Within 30–60 min	1.2–2.2 hours	4 hours	First-line
Clindamycin	900 mg	Within 30–60 min	2–4 hours	6 hours	$\beta$ -Lactam allergy (preferred)
Vancomycin	15 mg/kg	Within 120 min	4–8 hours	NA	$\beta$ -Lactam allergy; known MRSA colonization
Daptomycin	6 mg/kg	Within 30–60 min	8–9 hours	NA	Vancomycin allergy; known MRSA colonization; known vancomycin-resistant enterococci

\*Modified from Bratzler *et al.*<sup>362</sup> and from the American Society of Health-System Pharmacists, Bratzler *et al.*<sup>682</sup> and Berrios-Torres *et al.*<sup>15</sup>

†Adults with normal renal function.

MRSA, methicillin-resistant *Staphylococcus aureus*; NA, not available.

unnecessary. Consequently, adjustments for renal function in preoperative prophylaxis for interventional pain procedures or surgery are seldom needed. Preoperative oral antibiotics have been shown to reduce SSIs in complex dermatological procedures<sup>364</sup>; however, there are no studies directly comparing the rate of SSIs in patients receiving oral versus intravenous preoperative antibiotics in interventional pain procedures. In situations where preoperative intravenous antibiotics cannot be given, oral antibiotics may be considered, but there is a lack of evidence to support the use of oral over intravenous antibiotics. In addition, there is concern with oral antibiotics that adequate antibiotic concentrations may not be achieved at the surgical site, especially in higher risk surgical procedures (class D, see table 3).<sup>365</sup> Therefore, intravenous antibiotics are preferred for procedures where preoperative antibiotics are indicated.

There are no recommendations or evidence for the use of antibiotic prophylaxis in most routine interventional pain injections (ie, ESIs, facet blocks, RFA). Intradiscal antibiotics have been recommended for procedures requiring intradiscal access, because the administration of intravenous antibiotics does not reliably achieve adequate intradiscal concentrations.<sup>28 137</sup> However, ex vivo studies examining the effects of high antibiotic concentrations on cultured human intervertebral disc annular cells demonstrated deleterious effects on cell survival, cell proliferation, and metabolic rates, so these risks must be taken into consideration as well.<sup>366</sup>

#### Statements

- *Preoperative antibiotic prophylaxis has been shown to reduce the risk of SSIs. Level of certainty: high.*
- *Appropriate antibiotic selection includes determining the route of administration, weight-based dosing, and timing. Level of certainty: high.*

#### Recommendations

- *For class C and D procedures, appropriate preoperative intravenous antibiotic prophylaxis given 1 hour prior to surgical incision (2 hours for vancomycin) is recommended. Evidence: grade A.*
- *Vancomycin should only be used in patients colonized with MRSA or who are at high risk for MRSA. Evidence: grade A.*

#### Hand hygiene and skin antisepsis for procedural staff

Hand hygiene is a cornerstone in the prevention of HAIs.<sup>367 368</sup> Patient care advisories for specific procedures like neuraxial anesthesia emphasize preprocedure handwashing by the surgical team to help prevent SSIs.<sup>19</sup> Note that glove use should not be considered a substitute for hand hygiene, as bacterial multiplication still occurs under gloves, and gloves may develop holes or tears. Although specific evidence on hand hygiene in regional anesthesia and interventional pain medicine is limited, strong evidence links hand contamination to HAIs.<sup>248–254 260 262 271</sup>

Contamination of intravenous catheter ports occurs in up to 32% of cases, significantly associated with increased morbidity and mortality.<sup>203 368</sup> This risk extends to regional/neuraxial anesthesia, highlighting the need for strict asepsis to prevent transmission of pathogens like *S. aureus*, *Enterococcus*, and Gram-negative pathogens.<sup>203 250–253 262</sup> These findings apply to regional/neuraxial anesthesia where intravenous catheters are inserted for administration of sedation and/or analgesia and pain catheters for insertion of local anesthetic.<sup>250</sup>

Among postoperative infection events that have been directly linked to anesthesia provider, 50% occur before surgical patient

care (eg, intravenous stopcock contamination).<sup>253</sup> An RCT demonstrated that improved hand hygiene compliance along with a multifaceted, perioperative infection control program can significantly reduce both contamination and infection rates by >80%.<sup>278</sup> As such, expert guidance for intraoperative infection control recommends that all anesthesia providers, including those who perform regional and neuraxial procedures, take necessary steps to improve hand hygiene compliance.<sup>278</sup>

Evidence indicates that no single hand hygiene agent is definitely best for reducing SSIs, although certain agents are preferred for specific conditions, such as soap and water for spore-forming infections. Some studies suggest chlorhexidine may be more effective than iodine, and alcohol more effective than aqueous solutions in reducing CFUs, but the findings have not directly correlated with clinical outcomes.<sup>249 367</sup>

The WHO and CDC guidelines emphasize the importance of hand hygiene in healthcare settings. WHO advises removing rings, wrist watches, and bracelets, and prohibiting false nails to prevent SSIs.<sup>369</sup> The CDC recommends no artificial fingernails or extensions in those who have direct contact with surgical or ICU patients, but does not make any explicit recommendations regarding jewelry.<sup>370</sup> Research associates artificial nails and jewelry with higher levels of Gram-negative bacteria and potential glove puncture risks, leading to national guidelines recommending jewelry removal before wearing sterile gloves.<sup>1 2 21 250 367</sup> However, intact nail polish is not considered a risk, although chipped polish is.<sup>12</sup> The Society for Healthcare Epidemiology/Infectious Disease Society of America/Association for Professionals in Infection Control and Epidemiology practice recommendations prohibit artificial nails for all healthcare workers, and advise against nail polish for those in the sterile field. Regarding jewelry and fingernail polish for non-scrubbed individuals, the recommendations defer to the individual facility or the institutional policy.<sup>367 371</sup> Notably, a Cochrane systematic review was able to identify only one study of fingernail polish and no studies of jewelry with respect to infections, suggesting that although there is no strong evidence against these items, their prohibition is reasonable and a generally accepted practice.<sup>372</sup>

#### Hand scrub time recommendations

Scrub time depends on the agent used and the corresponding manufacturers' recommendations, but alcohol-based scrubs require full coverage with enough time to dry. For non-surgical scrubs, soap and water need at least 15 s of thorough hand washing, while surgical antisepsis requires a minimum of 2 min.<sup>367</sup> Low-quality evidence suggests a 3 min scrub removes more CFUs than a 2 min one, but it is unclear if this impacts infection rates.<sup>372</sup> The benefits of nail brushes or picks are uncertain. However, NICE advises that for preventing SSIs, the surgical team should wash their hands with an antiseptic solution before the first operation of the day, using a single-use brush or pick for nails, ensuring cleanliness.<sup>368</sup>

#### Statements

- *Hand hygiene with skin antisepsis as a key component of a multifaceted antiseptic strategy decreases hospital-acquired infections, including SSIs. Level of certainty: high.*
- *For surgical hand scrubs, chlorhexidine-based solutions may be preferred over iodine-based options due to the improved ability to decrease bioburden (eg, CFU). Level of certainty: moderate.*
- *Except for specific clinical instances where soap and water are preferred (eg, Clostridioides difficile infections or visibly*

soiled hands), hand hygiene can be performed with a variety of agents, including alcohol-based scrubs. Level of certainty: moderate.

- ▶ Hand hygiene scrub time should be at least 15 s for non-surgical scrubs, and 2 min for surgical scrubs, allowing enough time for the skin to dry, in conjunction with manufacturers' instructions. Level of certainty: moderate.
- ▶ Jewelry, artificial nails, and chipped nail polish may increase the risk of HAIs and SSIs. Level of certainty: moderate.

#### Recommendations

- ▶ All procedural staff should perform hand hygiene prior to the first case of the day, before and after glove use, before and after patient contact, and any time hands are visibly soiled. Evidence: grade B.
- ▶ For alcohol-based scrubs, scrub time should be as long as indicated by the manufacturer, allowing for full coverage and adequate drying. For aqueous solutions, hand sanitizing times prior to type A and B procedures (ie, non-surgical scrubs, see table 3) should be at least 15 s, with more invasive procedural hand scrubs (ie, surgical scrubs) lasting at least 2 min prior to type C and D procedures. Evidence: grade B.
- ▶ Jewelry should be removed to optimize hand hygiene. Evidence: grade B.
- ▶ Artificial nails or chipped nail polish should be avoided. Evidence: grade B.

#### Aseptic technique procedural practices

##### General considerations

Several important components are critical to antisepsis including a surgical wardrobe, proper hand hygiene, antiseptic solution selection and application practices, the use of sterile drapes, and sterile preparation of medications.<sup>371 373–375</sup> While there is no universal standard, the complexity of aseptic precautions may need to be adjusted based on the specific risks of each patient or procedure.

##### Prevention strategies for epidural and spinal needle contamination

Migration of skin bacteria through the needle track is the major source of colonization of regional anesthesia insertion sites.<sup>376 377</sup>

Studies show that even with aseptic techniques and skin cleansing, the epidural space can still become contaminated by skin flora beneath the epidermis.<sup>376</sup> Raedler *et al*<sup>378</sup> discovered higher rates of epidural needle contamination in cases that required multiple passes for catheter insertion. It should be noted that this study omitted a requirement for wearing face masks and skin preparation used 10% polyvidone-iodine. Conversely, Orlikowski *et al*<sup>379</sup> did not find a similar link with difficult epidural insertions and bacterial contamination rates, possibly due to better sterile practices and the use of chlorhexidine 0.5% in 70% alcohol. The most frequently found skin surface bacteria are CoNS, such as *S. epidermidis* (65%–69%); however, *S. aureus*, which comprises 1%–2% of skin flora, is more frequently found in neuraxial infections.<sup>379</sup>

##### Surgical cap, mask, gloves

While no research specifically addresses the individual risks of wearing or not wearing a surgical cap or sterile gloves, both international and national guidelines consistently stress their importance for maintaining asepsis during procedures.<sup>14 19 373 375 380</sup> The provider, the patient, and any person involved with the procedure are suggested to wear a surgical cap or bonnet.

The effectiveness of wearing a surgical mask during procedures has been debated over the years,<sup>381</sup> but evidence links masking to a reduction in serious CNS infections associated with neuraxial anesthesia.<sup>55–57</sup>

Masking has been shown to reduce bacterial shedding<sup>382</sup> and offer protection from potential blood or body fluid exposure.<sup>373</sup> During regional anesthesia, all those present in the procedure area should wear a mask to minimize the risk of spreading infections. Philips *et al*<sup>383</sup> demonstrated a surgical mask does prevent bacterial dispersion (no growth of oral flora on agar plates at a distance of 30 cm), whereas bacterial growth occurred in 50% of plates in subjects talking without masks.<sup>383</sup> Masks that had been worn for ≥15 min were found to be less effective at protecting against dispersion compared with fresh masks, although this finding did not achieve statistical significance.<sup>383</sup> While not a universally accepted practice, using a fresh mask is advised, balancing the need against personal protective equipment shortages.<sup>383</sup>

The CDC and WHO recommend that mouth, nose, and eye protection be worn for all procedures when exposure to blood splashes is expected, and a surgical mask should be worn for all procedures performed in an OR,<sup>373 384</sup> particularly when accessing the spinal canal or subdural space.<sup>14 380</sup>

#### Impact of barrier protections (gowns)

The universal use of sterile gowns is controversial.<sup>19 373 375 385</sup>

Gowns are considered barriers that prevent cross-contamination of infectious material between providers and patients. That said, in most cases the only direct contact point with the patient are the sterile, gloved hands of the proceduralist. In an RCT involving 214 obstetric patients, no notable differences were demonstrated in the rates of epidural catheter-tip colonization between providers who wore a sterile gown along with a hat, sterile gloves, and a surgical mask, and those who did not wear gowns. This was observed despite the colonization rates exceeding 7% and the strict application of aseptic techniques.<sup>386</sup>

Implantable device procedures involving a skin incision and higher risk procedures (eg, discograms, SCS trials/implants) warrant adoption of full operating theater practices, including the use of a sterile gown and full sterile draping.<sup>387</sup>

#### Statements

- ▶ Aseptic technique standards for all classifications of regional anesthesia and pain medicine procedures include: hand hygiene, chlorhexidine-alcohol-based skin preparation, sterile draping, and use of sterile gloves, disposable cap, and surgical mask. Level of certainty: high.
- ▶ The role of impact barrier protections (gowns) in pain procedures is not well defined except in the case of procedures involving implanted devices. Level of certainty: moderate.

#### Recommendations

- ▶ Use of a hat and surgical mask should be employed for regional anesthesia and pain medicine procedures in class B, C, and D. Proceduralists should wear surgical cap and mask when performing procedures in an OR setting, including PNBs. Evidence: grade B.
- ▶ Sterile gloves should be used for all regional and pain medicine procedures (class A, B, C, and D). Evidence: grade B.
- ▶ Sterile gown use is not necessary during short-term continuous regional anesthesia procedures with an estimated duration of therapy of 4 days or less. Evidence: grade B.

- ▶ *Maximal barrier precautions (including use of sterile gowns) should be used for class C procedures. Evidence: grade C.*
- ▶ *Maximal barrier precautions (including use of sterile gowns) should be used for class D procedures. Evidence: grade B.*

### Patient skin antisepsis

Prior to application of a skin antiseptic, gross contamination around the incision site should be removed (CDC category IB).<sup>29</sup> Chlorhexidine gluconate, particularly when combined with alcohol, has been established as a highly effective antiseptic for skin preparation prior to surgical procedures. Its efficacy is backed by RCTs and meta-analyses that demonstrate its role in significantly reducing the incidence of SSIs, offering a more effective alternative to povidone iodine, especially in the context of clean surgery.<sup>388–391</sup> An RCT and multiple meta-analyses have shown that the use of chlorhexidine-alcohol significantly reduces the rate of SSIs and results in cost savings compared with povidone iodine.<sup>392–394</sup> In addition, WHO has provided strong recommendations, despite the evidence being of low to moderate quality, for the use of chlorhexidine-alcohol over aqueous povidone iodine or povidone iodine with alcohol for surgical skin preparation, highlighting its prominent role in SSI prevention.<sup>395</sup> However, a recent RCT demonstrated that povidone iodine when compared with chlorhexidine and both formulated with alcohol was non-inferior in preventing SSIs after cardiac or abdominal surgery.<sup>396</sup>

For interventional pain procedures, the US Food and Drug Administration (FDA) has not approved the use of chlorhexidine for neuraxial procedures due to a lack of clinical safety trials regarding possible neurotoxicity. However, the use of chlorhexidine for spinal anesthesia has not been shown to increase neurological complications.<sup>397</sup> Guidance in the UK recommends use of 0.5% rather than 2% chlorhexidine for neuraxial blocks.<sup>398</sup> The use of chlorhexidine prior to epidural catheterization has been shown to be superior to povidone iodine in reducing catheter colonization rates.<sup>399</sup> Although there are no studies directly comparing infection rates with the use of chlorhexidine gluconate versus povidone iodine for interventional pain procedures, based on extrapolation of data from other surgical subspecialties, chlorhexidine-based products may offer improvement in infection control rates.

### Statement

- ▶ *Chlorhexidine-alcohol has been shown to be superior to povidone iodine in reducing SSIs. When using chlorhexidine-alcohol, allow for adequate drying time and follow the manufacturer's and facility recommendations. Level of certainty: moderate.*

### Recommendation

- ▶ *Chlorhexidine-based products are the preferred skin antiseptic in surgical and interventional pain procedures (including neuraxial). Evidence: grade B.*
- ▶ *In individuals with allergic reactions to chlorhexidine-based products, povidone iodine formula with alcohol should be considered. Evidence: grade B.*

### Single versus multidose medication vials

#### Multidose vials and infectious risk

Multidose vials contain more than one dose of a medication and must be labeled as such by the manufacturer. In addition, they must meet antimicrobial effectiveness testing requirements but do not guard against viruses, fungi, or contamination from

improper injection practices.<sup>400</sup> Multidose vials are perceived to be more cost-effective, as they typically have a lower per-dose price and require less storage space.<sup>401</sup> Although studies have reported a low rate of microbial contamination in multidose vials,<sup>402–404</sup> there have been a number of bacterial and viral outbreaks related to the use of multidose vials,<sup>405–410</sup> as well as inappropriate use of single-dose vials for multiple patients.<sup>57 97</sup>

In most cases, vial contamination and infections were related to failure to follow standard precautions and aseptic technique. However, the largest outbreak of infections related to pain procedures was due to fungal contamination of methylprednisolone arising from a single compounding pharmacy, without evidence of widespread unsafe injection practices.<sup>114</sup>

The infectious risk of a multidose vial compared with its single-use counterpart depends on the intended procedure and the medication(s) used. Infection following neuraxial and deep peripheral blocks are often more serious and difficult to detect early on compared with superficial blocks. Thus, greater caution should be exercised when considering multidose vials for neuraxial or deep blocks compared with more superficial procedures. Local anesthetics have varying inherent antimicrobial properties that decrease with time and improper storage.<sup>411</sup> Although some medications include antimicrobial preservatives to extend sterility, their use in certain procedures remains controversial due to potential neurological risks.<sup>412</sup>

The CDC and WHO recommend prioritizing single-dose vials to minimize infection risks.<sup>373 413</sup> If multidose vials are to be used, they recommend following manufacturers' guidelines, using aseptic technique, and ensuring proper storage.<sup>413</sup> Similarly, WHO advises using multidose vials only if there is no alternative, dedicating multidose vials to a single patient whenever possible, storing the medication in a separate treatment or medication room, and discarding if sterility is compromised.<sup>373</sup> The US Pharmacopeia recommends dating the vial after initial opening or access, then discarding by the printed expiration date or within 28 days, whichever comes soonest.<sup>414</sup>

### Statements

- ▶ *Infectious outbreaks can occur with both single-dose and multidose medication vials. Level of certainty: high.*
- ▶ *Risk factors for infection related to injectable medication administration include failure to adhere to standard precautions and aseptic technique; improper manufacturing, compounding, or storage conditions; and inappropriate use of single-dose vials for several patients. Level of certainty: high.*
- ▶ *The infectious risk of a multidose vial compared with its single-use counterpart depends on the medication used (ie, inherent microbial properties), storage conditions, and adherence to multidose vial recommendations. Level of certainty: moderate.*

### Recommendations

- ▶ *The rubber septum on medication vials should be disinfected with alcohol prior to piercing. Evidence: grade B.*
- ▶ *Single-dose vials should not be used for multiple patients. Evidence: grade A.*
- ▶ *When possible, multidose labeled vials should be dedicated to individual patients. Evidence: grade B.*
- ▶ *In cases where single-dose vials are not available or feasible, use of multidose vials may be considered if they are stored according to manufacturer's recommendations, outside of immediate patient care areas, with the initial access date*

clearly labeled, and appropriate aseptic technique used for medication withdrawals as outlined by the CDC. Evidence: grade A.

- ▶ If a multidose vial with an FDA-approved label is used for multiple patients, then CDC recommendations should be followed, including disinfecting the vial by rubbing the diaphragm with alcohol, drawing up all medications in a clean medication preparation area, following expiration dates, and keeping multidose vials outside of the vicinity of the patient treatment area. A multidose vial must be discarded if sterility is compromised or questionable. Evidence: grade A.

Table 8 summarizes the preprocedural recommendations.

## Procedural recommendations

### Optimization of operating room environment

Few clinical studies directly address how the OR environment might limit SSIs and none specifically included neuromodulation procedures. A study by Bohl *et al*, examining the impact of OR traffic on SSIs in 1944 cases, found no difference in infection rates between low-traffic and regular-traffic rooms, suggesting that while OR personnel and traffic can increase contamination, traffic control alone may not reduce SSIs.<sup>415</sup> However, OR personnel can be a major source of contamination in the OR. In addition, the number of personnel, as well as traffic flow rates in the OR, positively correlate with the degree of airborne contamination. Therefore, efforts should be made to limit OR traffic.<sup>416 417</sup>

Modern ORs are typically designed with high-efficiency particulate air (HEPA) systems intended to reduce contamination by directing airflow away from the patient.<sup>418–425</sup> However, studies indicate that while laminar airflow can decrease bacterial presence, it does not necessarily correlate with lower SSI rates.<sup>426–431</sup> Although there is little evidence that potential disruption in laminar air flow increases risk of infection, there is reasonable evidence that the number of individuals present in a room, their behavior, and the frequency of door openings can increase the counts of airborne bacterial CFU,<sup>431–437</sup> which may explain increased risk of infection in observational studies.<sup>426 438</sup>

Operating room temperature is generally between 68°F and 73°F (20°C and 23°C).<sup>439</sup> Maintaining patient normothermia is essential as hypothermia can increase SSI risks, especially in colorectal or trauma surgeries.<sup>439–442</sup> Optimal humidity levels are considered to be between 30% and 60% to minimize bacterial growth without compromising provider comfort.<sup>439</sup> Increased surgical duration is a clear risk factor for SSI development,<sup>443</sup> with obvious increases in a multitude of exposure risks (ie, bacterial transmission events).<sup>250 251 444</sup>

### Statements

- ▶ The impact of laminar flow in the OR on risk of infection is uncertain. Level of certainty: low.
- ▶ Although currently there is no clear evidence that OR HEPA filtration decreases SSI, there is evidence that HEPA reduces air CFU. Level of certainty: moderate.
- ▶ Operating room humidity levels influence bacterial growth rates, particularly in excess of 70% humidity. Level of certainty: moderate.
- ▶ Low OR temperatures are associated with increased risk of infection if this contributes to perioperative patient hypothermia. Level of certainty: moderate.
- ▶ Increased OR traffic increases SSI risk. Level of certainty: moderate.

- ▶ Increased procedure time has been shown to increase the risk of SSI. Level of certainty: moderate.
- ▶ In operating rooms, the minimum air movement requirement is 15 total air changes per hour. Level of certainty: moderate.

### Recommendations

- ▶ Operating rooms should have HEPA filtration systems. Evidence: grade B.
- ▶ Maintain OR humidity levels between 20% and 70% to decrease bacterial growth. Evidence: grade B.
- ▶ Avoid unnecessary delays that result in increased procedure duration to reduce the risk of SSI. Evidence: grade A.
- ▶ Minimize OR traffic to reduce the risk of SSI. Evidence: grade C.

### Recommendations for use of fluoroscopy

The C-arm is a potential source of contamination. Multiple areas of the C-arm are potential sources of contamination. Furthermore, contamination of the sterilely covered light handle has been reported to be as high as 14.5%.<sup>416 445</sup> Biswas *et al* evaluated the sterility of 25 C-arm drapes placed with aseptic technique after being used during spine surgery and found that all locations were contaminated at the end of the case with the front, top half, and superior end of the image intensifier having the highest rates of contamination.<sup>446</sup> Peters *et al* published a single-cohort study using 30 consecutive patients undergoing operative fracture fixation and cultured the C-arm drape every 20 min.<sup>447</sup> They also looked at number of personnel in the OR, number of door openings, and C-arm position changes. They found that there was a 17% contamination rate on initial draping, 50% at 20 min, 57% at 40 min, and 80% at 80 min. Time until contamination was shorter for cases where there were more lateral position changes.

### Statements

- ▶ The C-arm has a high contamination rate. Level of certainty: moderate.
- ▶ C-arm contamination rate increases with operating time and number of lateral position changes. Level of certainty: moderate.

### Recommendations

- ▶ Sterile C-arm covers should be used in open, invasive procedures and procedures where there is a high risk of the instruments touching the image intensifier. Evidence: grade B.
- ▶ Care should be taken to avoid contacting the C-arm even when a sterile cover is placed. Evidence: grade B.

### Recommendations for ultrasound-guided regional anesthesia and pain procedures

Ultrasound imaging is a useful diagnostic and procedural tool in a variety of medical settings and its utilization continues to grow. When performing ultrasound-guided interventional and diagnostic procedures, it is important to limit the risk of infection. Ultrasound-guided procedures provide several additional opportunities for cross-infection of patients, ranging from poor hand hygiene to probe, cord, and keyboard contamination, despite low-level disinfection (LLD), and the use of contaminated coupling gel.<sup>448–450</sup> Globally, these infection concerns have resulted in the development of ultrasound-specific infection control recommendations.<sup>14 451–456</sup> Guidelines have originated from Health Canada, the Australian Sonographers Association,<sup>457 458</sup> and from the USA, including from the CDC, the

**Table 8** Preprocedural recommendations for reducing SSIs

Recommendations	USPSTF grade*	Recommendations based on procedure type†				Comments
		A	B	C	D	
Patient risk factors for infection should be assessed, discussed, and modified when possible, prior to offering the procedure to appropriate candidates.	C	✓	✓	✓	✓	
Identify and optimize patient risk factors (eg, tobacco use, diabetes mellitus) prior to implantable device therapy surgeries.	B			✓	✓	
Avoid intra-articular steroid injections within 1 month of planned replacement surgery for that joint.	D	✓				
Discuss with the surgeon the risks/benefits when considering intra-articular steroid injections in a joint planned for replacement surgery within 3 months.	C	✓				
Intra-articular steroid injections to the knee should not be offered following total knee arthroplasty.	D	✓				
Intra-articular steroid injections to the hip should not be offered following total hip replacement.	D	✓				
The decision to perform single-injection regional nerve blocks in patients with localized well-controlled infections should be decided on a case-by-case basis if these blocks are not performed near the infected site. The safety of continuous catheters in such patients is unknown and, hence, not preferred.	I	✓				
Prolonged use of regional nerve block catheters may increase the risk of infection. Extended use beyond 4–5 postprocedure days should be decided based on the risk-to-benefit profile of continuing such therapies while carefully monitoring for any signs and symptoms of infection.	C		✓	✓		
Externalized neuraxial catheters beyond 2 weeks should be avoided when possible, to reduce the risk of meningitis.	B			✓		
Perioperative blood glucose should ideally be maintained at ≤150 mg/dL for implantable device surgeries.	B				✓	
Patients should be tested for <i>Staphylococcus aureus</i> (MRSA and MSSA) using a nasal swab, and decolonization should be performed in colonized patients prior to pain device implantation.	B			✓	✓	
In individuals known previously to be MSSA or MRSA carriers, decolonization should be repeated prior to additional procedures beyond 10 days from initial decolonization.	C			✓	✓	
When performing decolonization, use mupirocin nasal application and chlorhexidine body scrubs for 5 days in patients screening MSSA-positive or MRSA-positive to reduce SSI. The decolonization should occur no earlier than 10 days prior to the planned surgery.	B			✓	✓	
Neuraxial block: stopping the biologic drug and/or targeted DMARD should be considered with a neuraxial corticosteroid injection (epidural, facet joint, sacroiliac joint). If a patient is taking a conventional synthetic DMARD with an oral corticosteroid, discontinuation of these drugs should also be considered.	C		✓			
Surgical interventional pain procedures (IT pumps, SCS implantation): stopping the biologic drug and/or targeted DMARD should be considered with surgical interventional pain procedures. If a patient is taking a conventional synthetic DMARD with an oral corticosteroid, discontinuation of these drugs should be considered.	C				✓	
Hand washing with soap and water or an alcohol-based hand rub prior to the first case of the day, before and after glove use, before and after patient contact, and any time hands are visibly soiled.	B	✓	✓	✓	✓	
Use of aqueous-based hand sanitizer for at least 15 s.	B	✓	✓			
Use of alcohol-based scrubs for manufacturer recommended time or surgical hand scrub for at least 2 min.	B			✓	✓	
Hand and arm jewelry should be removed.	B	✓	✓	✓	✓	
Artificial and chipped nail polish should be avoided.	B	✓	✓	✓	✓	
Appropriate preoperative intravenous antibiotic prophylaxis given 1 hour prior to surgical incision (2 hours for vancomycin) is recommended.	A			✓	✓	Prophylactic intradiscal and intravenous antibiotics have not been shown to conclusively decrease the rate of discitis in humans. <sup>136 137 683 684</sup> In addition, high intradiscal antibiotic concentrations may affect intradiscal cell survival, cell proliferation, and metabolic rates. <sup>366</sup> Therefore, a risk-benefit analysis should be considered prior to administration for intradiscal procedures or following inadvertent disc penetration following another procedure such as a transforaminal epidural steroid injection.
Vancomycin should only be used in patients colonized with MRSA or who are at high risk for MRSA.	A			✓	✓	
Do not perform hair removal routinely prior to procedures.	A	✓	✓	✓	✓	
If hair is removed, use electric clippers immediately before surgery.	A	✓	✓	✓	✓	

\*Grades are described in table 1. A represents the highest level evidence and I (insufficient) the lowest.

†Procedures are classified in table 3.

DMARD, disease-modifying antirheumatic drug; IT, intrathecal; MRSA, methicillin-resistant *S. aureus*; MSSA, methicillin-susceptible *S. aureus*; SCS, spinal cord stimulation; SSI, surgical site infection; USPSTF, US Preventive Services Task Force.

American Institute of Ultrasound Medicine (AIUM), the Society of Hospital Medicine, and from Europe, including the European Society of Radiology Ultrasound Working Group.<sup>14 456 459–462</sup> Unfortunately, a high degree of non-compliance with practice recommendations exists.<sup>463–466</sup>

The current literature emphasizes the need for education, training, practice of safe disinfection, and cleaning methods for ultrasound equipment to reduce infection risk. All ancillary equipment should be cleaned on a regular basis, with emphasis on transducers for every procedure to minimize infection risk. Safe handling of equipment with LLD should be widely used and recommended for ultrasound-guided regional and pain procedures.<sup>456 467 468</sup>

### Ultrasound transducer

Ultrasound equipment, and in particular ultrasound transducers (probes)<sup>201 221</sup> can be a source of nosocomial infections (bacterial and viral) in patients undergoing interventional and diagnostic procedures. When not covered with a transducer cover, the transducer can come into direct contact with the patient. Coupling agent or gel can also be a vector for infection transmission, and redundant gel on these transducers can allow bacteria and viruses to survive for hours to months on surfaces, depending on the pathogen.<sup>469</sup> For example, *S. aureus* duration of persistence is 7 days to 7 months and hepatitis B virus duration of persistence is >1 week.<sup>456</sup> Multiple studies have demonstrated the risk of contamination and the risk of cross-infection through ultrasound equipment. A study examining 100 consecutive patients undergoing routine abdominal/pelvic ultrasound scans demonstrated that in 13% of the procedures the probes were colonized with *S. aureus*.<sup>201</sup> In addition, in 7% the contaminating strain was the same bacteriophage type as that isolated from the patient either before or after the examination (ie, interpatient transfer). In individuals who were colonized with *S. aureus* prior to the ultrasound examination, after scanning 21% of the probes became colonized with the same phage type. In another study examining 44 transducer heads, 27% were contaminated.<sup>470</sup> Fowler and McCracken in a prospective study on 40 patients demonstrated that on average 128 CFUs were transferred by unclean probes.<sup>471</sup> In addition, when a patient in this study was known to have MRSA, the transmission rate of MRSA was 41%. Published guidelines and recommendations are available to limit and prevent these infections. It is important that the national and institutional recommendations are followed, and the latest evidence be incorporated as guidelines change.

The Spaulding classification describes a rational approach to sterilization and disinfection of medical equipment/devices according to the degree of risk of infection as critical, semicritical, and non-critical (table 9).<sup>472</sup> According to this classification, ultrasound-guided regional anesthesia and pain procedures can be classified as non-critical (ie, non-invasive, contact of ultrasound transducer with intact skin), or semicritical (objects

that contact mucous membranes or non-intact skin) based on the procedure environment and technical aspects. The critical classification is reserved for objects that enter normally sterile tissue or the vascular system. The semicritical classification is associated with endocavitary/internal transducers like transrectal, transvaginal, and transesophageal probes compared with external transducers used for regional anesthesia and pain procedures.<sup>473–476</sup> Single-use sterile ultrasound cover and sterile ultrasound gel are recommended for every LLD procedure. Caution should be exercised with some transducer covers as they have been shown to contain microperforations and can tear, so the use of a transducer cover does not change the Spaulding classification or disinfection process.

For the protection of patients, preparation of all transducers should have a systematic process for cleaning, disinfection, and storing. Cleaning with soapy water, sterile paper towels, and ethanol-soaked wipes will help remove all the visible gel, biofilm, and soil on the transducers. LLD with quaternary ammonium compounds, alcohols, and phenols helps inactivate most vegetative bacteria, all enveloped viruses, some non-enveloped viruses, and most fungi, except bacterial spores, and has shown reduction in bacterial contamination for non-critical procedures.<sup>477–480</sup> High-level disinfection (HLD) with substances like glutaraldehyde, hydrogen peroxide, peracetic acid, hypochlorite, phenol, and hibidil can remove all microorganisms except bacterial spores, and is effective against high-risk pathogens.<sup>481</sup> Sterilization of ultrasound transducers makes possible complete removal of all viable microorganisms, including bacterial endospores, but is impractical due to the heat sensitivity of the transducers, and robust HLD can be used as an alternative in these cases. Manufacturer's instructions for use can also enable guidance on reprocessing of transducers. If at any time the non-critical classification becomes semicritical or critical, then HLD should be used to prevent infection risk. Procedures performed under surgical conditions and interventional implant pain procedures should follow HLD for disinfection of transducers along with sterile transducer cover and sterile gel.

Numerous international guidelines classify ultrasound probes used for regional anesthesia as semicritical medical devices and call for sterile probe cover use in addition to HLD.<sup>454 465 482</sup> A recent intersocietal position statement has called for clarity, and reinforced the point that when ultrasound-guided percutaneous procedures that are imaged through intact skin and in conjunction with a probe cover (such as regional anesthesia and pain interventions), probes can be subjected to LLD and not the HLD suggested by many other guidelines.<sup>483</sup> The exception to this rule is if the probe comes into contact with blood or body fluids; in such cases, HLD must be employed.

In conclusion, LLD is effective for the disinfection of ultrasound transducer or probe during regional and pain procedures, while HLD is reserved for critical instruments and internal transducers.<sup>468 484 485</sup>

**Table 9** Spaulding classifications and low-level or high-level disinfection<sup>472</sup>

Spaulding classification	Risk of contact	Disinfection	Agents used	Organisms inactivated
Non-critical	Only with intact skin	Low-level disinfection (LLD)	Quaternary ammonium compounds, alcohol, phenol	Vegetative bacteria, enveloped viruses, some non-enveloped viruses, fungi
Semicritical	With mucous membranes or non-intact skin	High-level disinfection (HLD)	Hydrogen peroxide, peracetic acid, glutaraldehyde, hibidil, hypochlorite	All microorganisms
Critical	With sterile tissues	Sterilization	Glutaraldehyde, hydrogen peroxide, peracetic acid, ethylene oxide gas	All viable microorganisms, bacterial spores

## Statements

- ▶ The ultrasound transducer can be a vector for infection. Level of certainty: high.
- ▶ LLD is effective for disinfection of a transducer used for non-critical procedures with intact skin (eg, diagnostic ultrasound over intact skin areas). Level of certainty: high.
- ▶ HLD is effective for disinfection of the transducer used for semicritical (ie, mucous membranes and non-intact skin) procedures. Level of certainty: high.

## Recommendations

- ▶ Safe handling of ultrasound equipment with LLD should be widely used and recommended for ultrasound-guided regional and pain procedures. Evidence: grade B
- ▶ Transducers must be cleaned/disinfected before first use and after every procedure. Evidence: grade B
- ▶ Thorough cleaning and disinfection of all ultrasound transducers are essential for every procedure to interrupt significant cross-contamination risk. Evidence: grade B.
- ▶ Non-critical procedures (eg, diagnostic ultrasound over intact skin areas) with intact skin can be safely performed with LLD of the transducer. Evidence: grade B.

## Ultrasound gel

Another vector for infection is ultrasound gel.<sup>14 456 466 486–494</sup> Multiple published case reports identify ultrasound gel as a source of nosocomial infection.<sup>488 489 495–500</sup> In these case reports, both manufacturer and user processes are sources of bacterial and fungal infections. Causative organisms include *Achromobacter xylosoxidans*,<sup>490</sup> *Burkholderia cenocepacia*,<sup>501</sup> *Burkholderia cepacia*,<sup>488 489 495–500</sup> *Klebsiella pneumoniae*,<sup>487</sup> *Mycobacterium massiliense*,<sup>502</sup> and *S. aureus*.<sup>503</sup> Hutchinson *et al*<sup>488</sup> identified serious *B. cepacia* infections at tertiary care centers that resulted from intrinsically contaminated ultrasound gel that originated directly from the manufacturer.<sup>488</sup> Respiratory infections from *P. aeruginosa* occurred in patients who had undergone cardiovascular surgery where intraoperative transesophageal echocardiography was used.<sup>504</sup> After an infection control investigation with the assistance of molecular typing, ultrasound gel multi-dose bottles were identified as the source of the *P. aeruginosa*. Furthermore, sealed unopened bottles also contained the same isolate of *P. aeruginosa*, suggesting that contamination occurred at the time of manufacturing. A postprocedure outbreak of *M. massiliense* soft tissue and bloodstream infections resulted from manufacturer-contaminated ultrasound gel.<sup>502</sup>

Ultrasound gel manufacturers have also attempted to limit gelborne contamination through the addition of stabilizing bacteriostatic preservatives such as parabens.<sup>488</sup> First introduced in the 1930s, parabens (alkyl esters of *p*-hydroxybenzoic acid) are a type of preservative used in cosmetic, pharmaceutical, and industrial products that were thought to have significant bacteriostatic (stopping the growth or multiplication of bacteria) rather than bactericidal (destroying bacteria) effects. Examples of parabens include methylparaben, ethylparaben, propylparaben, and butylparaben. Although parabens are thought to have a broad spectrum of inhibiting activity against yeast, fungi, and bacteria, multiple reports have demonstrated resistance to these agents and ultimately questioned their bacteriostatic effects.<sup>466 488 505–509</sup> In 1995, Muradali *et al*<sup>508</sup> demonstrated that ultrasound gel containing parabens did not effectively limit the growth of *S. aureus*. A more recent study suggests that ultrasound gel containing parabens is only marginally effective at inhibiting the growth of specific bacterial species on a growth-promoting

substrate.<sup>466</sup> In this study, the ultrasound gel containing parabens was more effective at inhibiting the growth of Gram-positive bacteria (specifically *S. aureus* and MRSA) than Gram-negative bacteria (specifically *E. coli*, *K. pneumoniae*, and *P. aeruginosa*). The bacteriostatic effects of ultrasound gel containing parabens did not inhibit the growth of *P. aeruginosa* and only limited the growth of *E. coli* and *K. pneumoniae* for 24 hours. Gram-negative bacteria have been shown to have the ability to degrade, hydrolyze, and develop resistance to parabens.<sup>488 509 510</sup>

Besides contamination at manufacturing, ultrasound gel may spread infection through inappropriate use of products. An outbreak of *A. xylosoxidans* associated with ultrasound gel used for transrectal ultrasound-guided prostate biopsies occurred from contaminated ultrasound gel through which biopsy needles passed.<sup>490</sup> The ultrasound gel originated from a large supply bag that was used to refill ultrasound gel containers. In addition, nosocomial outbreaks of *K. pneumoniae* in six adult women and two neonates, and *B. cepacia* in a pediatric institution, have occurred secondary to inappropriate user processes for handling ultrasound gel.<sup>487</sup>

Ultrasound gel also serves as a vector for infection in non-invasive diagnostic procedures. The healthcare community often assumes that when non-invasive diagnostic ultrasound scans are performed on patients with intact skin, ultrasound gel is a non-critical item and sterility is not essential.<sup>460 511</sup> However, significant infections have occurred even in these situations. Weist *et al*<sup>503</sup> reported MSSA infections in neonates undergoing non-invasive hip ultrasound examinations that were associated with contaminated dispensing spatula and gel bottles.

Numerous factors can contribute to the risk of contaminating ultrasound gel and thus increase the spread of infection. For example, when using non-sterile ultrasound gel, multiple inappropriate practices may increase the risk of infection, including: (1) failing to wipe the outside of the bottle with a disinfectant between patients; (2) not following the expiration date of a bulk refilling container; (3) placing the tip or dispensing nozzle of the ultrasound gel bottle in direct contact with a patient, environment, or instrumentation; (3) reusing the ultrasound gel bottle after scanning individuals with known contact precautions; (4) refilling an ultrasound gel bottle by inserting the tip of the refillable bottle into the bulk container to aspirate contents; and (5) using inappropriate gel warming methods.<sup>462</sup> Refilling ultrasound gel bottles from larger containers is no longer recommended.<sup>458</sup>

To reduce gelborne contamination, multiple medical associations and government agencies have published warnings and proposed preliminary clinical recommendations to minimize infection when using sterile and non-sterile medical gels. In 2004, following several cases of bacteremia and septicemia that occurred from the utilization of contaminated ultrasound gel, Health Canada published practice recommendations for the use of both sterile and non-sterile gels.<sup>462</sup> These recommendations have been endorsed by many professional associations, including the Canadian Society of Diagnostic Medical Sonographers, the Society of Diagnostic Medical Sonography, and the AIUM. In April 2013, the Australian Sonographers Association published a background paper on the safe use and storage of ultrasound gel to prevent nosocomial infections, including cross-infections, and new guidelines were issued in February and May of 2021.<sup>457</sup> The stimulus for the background paper originated from the safety alerts and recalls released in 2012 by the Australian Department of Health Therapeutic Goods Administration due to the confirmed presence of bacterial contamination in ultrasound gel. In the USA, recommendations based on expert opinion had been proposed to minimize clinical risk.<sup>460</sup> These recommendations

build on the Health Canada recommendations that suggest using single-use sterile gels for invasive procedures involving neonates, for all procedures involving sterile equipment or non-intact skin, and for procedures on intact mucous membranes. Additional recommendations were proposed by Oleszkowicz *et al*<sup>460</sup> and a 'call' was made for the development of standardized professional society guidelines on the appropriate use of ultrasound transmission gel that could be adopted by healthcare practitioners and facilities. Recently, practice recommendations for ultrasound gel have originated from the CDC and the AIUM.<sup>461 512</sup>

Based on this information, it is clear that ultrasound gel serves as a vector for infection for both diagnostic and interventional pain procedures. When the appropriate steps are taken, the risk of infection is low.<sup>221</sup>

### Statements

- ▶ *Non-sterile ultrasound gel is a vector for bacterial and viral infections. Level of certainty: high.*
- ▶ *Parabens are ineffective in limiting bacterial growth, especially for Gram-negative bacteria. Level of certainty: high.*

### Recommendations

The following recommendations from published practice guidelines should be followed to limit the risk of infection.<sup>14 455 457 459–462 504 513</sup>

*Single-dose sterile ultrasound transmission gel should be used during the following:*

1. Performing regional anesthesia and/or interventional pain procedures.
2. Performing a biopsy or puncture.
3. Procedures involving mucous membranes (eg, transesophageal echocardiogram).
4. Scanning non-intact skin.
5. Scanning near a surgical wound.
6. Scanning neonates and critically ill pediatric patients.

*Evidence: grade A.*

*Non-sterile ultrasound gel may be used for low-risk, non-invasive procedures on intact skin and for low-risk patients. The following steps should be taken:*

1. *Single-use containers are recommended.*
2. *Avoid direct contact between the gel container dispensing tip and ultrasound equipment and patient.*
3. *Limit warming of ultrasound gel. Dry heat is the only recommended method. The warmer should be cleaned and disinfected regularly according to manufacturer's and infection control's policy requirements.*
4. *Additional multidose non-sterile ultrasound containers precautions include:*
  - a. *Seal multidose non-sterile ultrasound containers appropriately when not in use.*
  - b. *Discard multidose vials after being deployed on a patient who is under droplet or contact precautions.*
  - c. *Do not reuse ultrasound gel containers and replace when empty.*
  - d. *Bottle should be dated and discarded after 1 month of use.*
  - e. *Products must be stored in areas that are protected from potential sources of contamination.*

*Evidence: grade A.*

### Ultrasound probe covers

Whether ultrasound-guided PNBs necessitate the use of a sterile cover, non-sterile cover, or indeed any cover at all has been the subject of much debate. The absence of large, multicenter RCTs

comparing probe cover techniques means most of the limited information available is based on professional opinion and society guidelines.

In their retrospective review of 10 years of practice and 7500 ultrasound-guided single shot blocks at a single institution, Alakkad *et al* demonstrated that the use of LLD of a probe and a sterile, transparent, film-barrier dressing was associated with zero block-related infections.<sup>221</sup> This probe cover technique was used in conjunction with prepping of the procedure site using povidone iodine or chlorhexidine with 70% isopropyl alcohol, sterile gel to the skin, and sterile gloves. It is not clear to what extent each of those interventions contributed to these results.

It has been demonstrated that visibly clean ultrasound probes can still carry a significant amount of clinically relevant bacterial burden,<sup>491 494</sup> and that bacteria can survive on ultrasound transducers from several days to several months.<sup>456 491</sup>

The AIUM has revised guidelines for cleaning and preparing ultrasound transducers and equipment between patients.<sup>461</sup> The guidelines state that interventional percutaneous procedures such as regional anesthesia and pain interventions necessitate the use of a single-use probe cover, the sterility of which should be dictated by the procedure sterility. These guidelines, in addition to other similar recommendations, additionally state that in patients with COVID-19 infections requiring aerosolization procedures, an ultrasound cover should be used irrespective of the ultrasound procedure being performed.<sup>461 514</sup>

In a position statement on ultrasound in COVID-19, the World Federation for Ultrasound in Medicine and Biology Safety Committee acknowledge that miniature handheld ultrasound devices, connected to telephones or tablet devices are often used with COVID-19 patients, and state that where possible, the handheld transducer should be placed connected to the phone or tablet within a sterile transducer cover sleeve.<sup>515</sup> The same statement also suggests that it is mandatory to use traditional ultrasound probes in conjunction with single-use transducer covers.

Probe cover use is also recommended and supported by the updated guidelines on disinfection and sterilization in healthcare facilities from the CDC.<sup>513</sup> The use of probe covers does not change the Spaulding classification or the disinfection process, as probe covers may have microperforations, can break open and tear and, therefore, fail; probes should still be cleaned and disinfected between uses.<sup>513 516</sup> Historically, it has been noted that condoms were superior to commercially available probe covers (1.7% leakage vs 8.3% leakage for traditional covers),<sup>14 513</sup> but this finding has recently been called into question. A large, multisite study that evaluated 5000 probe covers and condoms during transvaginal ultrasound scans determined that non-latex commercial covers (0%–1%) had a lower failure rate than for latex commercial covers (0.6%–5%) and latex (0.4%–2.6%) and non-latex condoms (13%).<sup>517</sup>

In support of sterile probe covers for continuous techniques, a prospective, single-center evaluation of 760 ultrasound-guided nerve catheters, all of which were placed using full aseptic technique including a sterile probe cover, revealed a catheter colonization rate of 10.4% (95% CI 8.2% to 14.4%), and an infection rate of only 0.13% (95% CI 0% to 3.8%).<sup>37</sup>

The Australasian Society for Ultrasound in Medicine and Australasian College for Infection Prevention and Control produced collaborative guidelines on reprocessing ultrasound transducers in 2017.<sup>518</sup> They definitively recommend the use of sterile probe covers for ultrasound-guided invasive procedures, where the needle is close to the ultrasound transducer or cover, and contamination with blood or body fluid is possible.

There is at least moderate evidence that the net benefit of sterile probe covers is small.<sup>519 520</sup> There are no RCTs comparing sterile versus non-sterile sheaths with respect to infection rates.<sup>518 521</sup>

Many ultrasound practitioners are already using sterile, transparent, adhesive-film dressings as substitutes for probe covers, and this practice has been recognized in previous guidelines for single-shot blocks.<sup>522</sup>

The AIUM guidelines additionally state that if a probe cover is indicated but not available, then medical gloves or other physical barriers such as compatible medical dressings should be used.<sup>461</sup> The main focus relates to the pore size of the barrier being used. Sheaths with pore sizes of <30 nm are available and are effective at blocking most viruses. In support of this are the results of a single-center retrospective study where a sterile film dressing used as a probe sheath for nearly 7500 blocks was not associated with any cases of infection.<sup>221</sup> There are to date no studies evaluating the effectiveness of a variety of probe sheaths or transducer covers used for ultrasound-guided interventions,<sup>518</sup> and there are specifically no studies looking at the effect of the porous nature of transparent film dressings on transmission of infection.

Guidelines from the American College of Emergency Physicians echo other recommendations on sterile single-use probe covers for ultrasound-guided interventions such as regional anesthesia.<sup>523</sup> These guidelines take the additional step of stating that sterile adhesive-film dressings may be considered an effective barrier and that they are effective against organisms larger than 27 nm.

Best practice recommendations from the European Society of Radiology Ultrasound Working Group<sup>456</sup> state that only dedicated ultrasound transducer covers of adequate quality (CE mark of quality testing or equivalent) should be used.

There are two additional points to consider: transparent dressings are not validated by ultrasound manufacturers or by the FDA for use as ultrasound probe covers; and, the use of a transparent adhesive film renders one hand non-sterile—this has implications for the insertion of indwelling devices.

#### Statements

- *Ultrasound probes, even when clean, can act as vectors for transmission of infectious material between individuals. Level of certainty: high.*
- *The use of sterile probe covers is likely beneficial when performing ultrasound-guided regional anesthesia and pain interventions. Level of certainty: moderate.*
- *Transparent adhesive film dressings are not endorsed by US manufacturers or approved by the FDA for use as ultrasound probe covers. Level of certainty: high.*

#### Recommendations

- *For regional anesthesia and interventional pain procedures that do not involve implanted or indwelling devices, use LLD with single-use sterile probe cover and single-use sterile gel. Evidence: grade B.*
- *For surgical procedures and interventional implant pain procedures, use HLD for probe disinfection with single-use, long sterile probe sheath and sterile gel. Evidence: grade B.*
- *Transparent film dressings should not be used in lieu of dedicated, manufacturer-approved, commercially available ultrasound probe sheaths. Evidence: grade I (insufficient).*

#### Probe sheath and peripheral nerve block catheters

The use of sterile transducer covers appears to be a standard practice for continuous regional anesthesia in most published

case series,<sup>37 166</sup> yet there are isolated case reports of infections despite use of full sterile sheaths.<sup>219 220</sup> That being said, the use of sterile probe covers seems prudent and sensible in line with a full aseptic technique.<sup>524</sup> A joint committee of three regional anesthesia societies for ultrasound-guided pain procedures has already recommended the use of long sheaths when placing indwelling devices.<sup>522</sup>

Recommendations on the use of ultrasound guidance for central and peripheral vascular access in adults already state that an aseptic technique, sterile gel, and sterile sheath should be used.<sup>459</sup> Therefore, it seems logical that a nerve catheter placed percutaneously should also require skin disinfection, strict aseptic technique, and the use of sterile probe covers during catheter placement in order to reduce catheter-related infections too.<sup>200 204 524</sup>

#### Statement

- *Peripheral nerve catheters have a greater incidence of catheter colonization compared with central neuraxial catheters and the incidence varies with the site of PNB catheter placement. Level of certainty: moderate.*

#### Recommendation

- *Ultrasound-guided continuous regional anesthesia and indwelling device insertion should be performed in conjunction with a long sterile transducer sheath, which covers the transducer and cable that are near the sterile field. Evidence: grade B.*

#### Recommendations for surgical technique

##### Surgical incisions

Trikha *et al* published a prospective, randomized, controlled, blinded study that investigated surgical outcomes of 184 patients randomized for undergoing single-blade or double-blade surgical incision use (different scalpels for superficial and deep incisions).<sup>525</sup> There was no difference in SSI rate between techniques. Okereke *et al*,<sup>526</sup> Shamim,<sup>527</sup> and Groot and Chappell<sup>528</sup> published randomized, controlled, double-blinded studies comparing scalpel with diathermy, and showing no difference in SSI rate. Rongetti *et al* conducted an observer-blind, randomized equivalence clinical trial of 133 patients undergoing scalpel skin incision or electrocautery skin incision.<sup>529</sup> SSI was reported in 7.4% of the scalpel group and 9.7% of the electrocautery group. Prospective case-control studies showed similar results in laparotomy<sup>530–532</sup> and cranial incisions.<sup>533 534</sup> Salami *et al* showed no difference in infection between harmonic scalpel or a cold knife.<sup>535</sup>

Regarding the use of electrocautery in deep tissue, Tsimoyiannis *et al* conducted a prospective randomized study that investigated the safety of lymphatic dissection with monopolar cautery versus ultrasonically activated coagulated shears (UACS) in 40 patients.<sup>536</sup> Rates of infection in both groups were similar, with three patients in the cautery group and one patient in the UACS group developing postoperative wound infections. Iannelli *et al* published an RCT of 60 patients that compared the use of the PlasmaJet System (PJS) and monopolar electrocautery for the treatment of dissection surfaces in patients who underwent corrective abdominoplasty following weight loss. One patient in the cautery group and no patients in the PJS group developed a seroma ( $p=0.48$ ).<sup>537</sup> An interventional cohort study investigating the incidence of seroma, a risk factor for SSI, in laparoscopic ventral hernioplasty following monopolar cautery (five cases) or harmonic scalpel (20 cases) found that cauterization

of the hernia sac may prevent seromas.<sup>538</sup> In 2002, Kumar and Crawford reviewed the literature, which advised that deep fascia should be cut by scalpel or scissor along the line of fibers as fascia is prone to sepsis. However, a midline incision may be done by electrocautery with minimal bleeding.<sup>539</sup> A 2012 review concluded that electrocauterization does not increase the risk of infection.<sup>540</sup> However, electrocautery should be avoided at the tissue surface.

#### Statements

- *Significant differences have not been demonstrated in SSI infections with the utilization of electrocautery. Level of certainty: moderate.*
- *There is no difference in SSI incidence when scalpel or cutting diathermy is used for skin incision. Level of certainty: moderate.*

#### Recommendation

- *Limit tissue trauma, maintain hemostasis, eradicate dead space, and avoid the electrocautery at tissue surface. Evidence: grade B.*

#### Local anesthetic with epinephrine

Eighty-four studies were identified that met quality criteria and none discussed neuromodulation. Blome-Eberwein *et al* conducted a prospective, randomized, patient-blinded, controlled trial of 10 patients with second-degree or third-degree burns undergoing donor graft harvest at two donor sites.<sup>541</sup> Each patient received epinephrine at one site and plain saline at the other site and only one patient developed infection at either the epinephrine or plain saline site. Panneerselvam *et al* conducted a double-blinded RCT on 50 adults investigating the effect of lidocaine with epinephrine and lidocaine without epinephrine on wound healing after premolar extraction. No adverse events were reported.<sup>542</sup> Sveen carried out an observational study on 32 adults investigating the addition of epinephrine to local anesthetic and resulting outcomes after molar removal; no differences in healing between groups were noted.<sup>543</sup>

#### Statement

- *The addition of epinephrine to the local anesthetic preparation does not increase the risk of infection in surgical procedures. Level of certainty: low.*

#### Surgical time

A total of 386 studies were identified and 28 met our search criteria. Two retrospective series focused on neuromodulation. One evaluated the skill of operators and one examined OR duration. Of the other 26, we included only the 11 prospective series.

Rudiger and Thomson retrospectively reviewed 84 patients who underwent SCS. The study found that more skilled operators had lower infection rates (1.8%) compared with less skilled operators (13%), thus suggesting that experience improves efficiency and decreases SSIs.<sup>544</sup> Engle *et al* performed a retrospective chart review of 131 patients who received 142 implantable devices. The study investigated infectious complications following IDD and SCS. Cases that developed infection had a significantly longer surgical time (215 min) compared with those without infection (132 min).<sup>545</sup>

Harbarth *et al* conducted a prospective RCT of 21754 patients investigating risk factors of MRSA SSIs. Surgical duration greater than the 75th percentile was associated with a 50% MRSA SSI rate. However, there was no difference in the

incidence of overall infections in the control and intervention groups.<sup>546</sup> Case-control studies included Anderson *et al*, which showed that MRSA infections were more common in longer cases than MSSA infections or no infections.<sup>547</sup> Chen *et al* showed longer durations to be associated with a higher rate of MSSA infections.<sup>548</sup> Maragakis *et al* was a case-control study that compared 104 patients with SSI after spinal surgery with 104 control patients without SSI after spinal surgery. The study found that prolonged surgical duration was an independent risk factor for SSI after spinal surgery.<sup>549</sup> Boston *et al* showed similar results in spinal surgery patients.<sup>550</sup>

Observational studies included Kasatpibal *et al*, a prospective study of 8764 patients undergoing major operations in Thailand, where prolonged surgical duration correlated with increased SSI rates.<sup>551</sup> Hijas-Gómez *et al* showed that in 892 spinal fusion patients, a duration of surgery higher than the 75th percentile was a predictive factor for SSI.<sup>552</sup> Others found similar correlations in other types of surgery.<sup>553–556</sup>

In conclusion, surgical time should be optimized to reduce time spent in the OR. Longer procedure times have been associated with higher infection rates.

#### Statements

- *Increased procedure duration in surgical cases likely increases wound infection rates. Level of certainty: moderate.*

#### Recommendation

- *Avoid unnecessary delays that result in increased procedure duration. Evidence: grade B.*

#### Double gloving

Currently, there are no direct studies comparing the risk of SSIs with single gloving versus double gloving. However, double gloving has been shown in multiple studies to reduce the number of inner glove perforations. Surgical glove perforations are associated with SSIs. Tanner and Parkinson<sup>557</sup> and Mischke *et al*<sup>558</sup> in their Cochrane reviews found significant evidence that double gloving reduces innermost glove perforation and exposure to bloodborne pathogens. The Cochrane review by Tanner and Parkinson suggested that there was a reduction in exposure to bloodborne pathogens from 11% in the single-gloving studies to approximately 3% in the double-gloving studies.<sup>557</sup> This finding was supported in the subsequent Cochrane review by Mischke *et al*<sup>558</sup> and, as such, the Cochrane database suggests no further work concerning the use of double-gloving versus single-gloving needs to be considered. It is important to note that in neither review was the question of SSI reduction considered. Double gloving has moved into the realm of standard of care for surgical procedures involving an incision.

There have been questions regarding dexterity with double gloving. Hardison *et al* evaluated this question and found that there was no decrement in dexterity with double gloving.<sup>559</sup> This was supported by Sayin *et al* who also suggested that there was a tendency toward higher incidence of breach of the outermost glove in the left (or likely non-dominant hand).<sup>560</sup>

#### Changing gloves prior to handling implantable pain devices

There has been much discussion in the orthopedic and neurosurgical literature concerning the timing of glove changes and what events constitute highest risk. It has been widely suggested that changing gloves after draping and before skin incision should be strongly considered.<sup>561</sup> Kim *et al* reviewed eight studies evaluating microbiological contamination and perforation rate of

surgical gloves.<sup>562</sup> Based on these data, coupled with the finding that longer surgical time increases infection rate, the group recommended for joint arthroplasty that:

- ▶ outer gloves be changed after draping;
- ▶ outer gloves be changed before handling implants;
- ▶ outer gloves be changed every hour;
- ▶ outer gloves be changed if a visible perforation is observed.

Reviews of the literature from neurosurgical and general surgical sources, as well as from the neuromodulation literature, do not address the issue of timing of glove change to the extent that it is discussed in the orthopedic literature. The basic concept of double gloving requires reinforcement to the neuromodulation and interventional pain community since a recent questionnaire suggested that there is not universal adoption of this best practice.<sup>16</sup>

### Recommendations

- ▶ *Double gloving should be performed for procedures involving implantable devices. Evidence: grade B.*
- ▶ *Outer glove change should occur after noted perforation of the outermost glove. Evidence: grade A.*
- ▶ *Outer glove change by the surgeon and surgical staff is recommended following draping and prior to incision. Evidence: grade C.*
- ▶ *Outer glove change is recommended before implantable device handling, including manipulation of neuromodulation batteries/receivers and pumps. Evidence: grade C.*

### Wound irrigation

Wound irrigation (also referred to as surgical site irrigation) involves exposure of the site to a washing solution. There are several theories that have supported its clinical use to prevent SSI, including the removal of pathogens, damaged or necrotic tissue that could promote infection, and metabolic or deoxy-generated byproducts. When evaluating wound irrigation, the following variables should be considered including delivery method (ie, low-pressure vs high-pressure irrigation), volume, and solution additives.

Three RCTs examining no wound irrigation in comparison with wound irrigation with 0.9% saline or povidone iodine have reported conflicting findings regarding the potential to reduce SSI rates.<sup>563–565</sup> The earliest trial by Cervantes-Sánchez *et al* included adults and children undergoing appendectomy for acute appendicitis and noted that syringe pressure saline irrigation reduced SSI.<sup>563</sup> The later trials in women undergoing cesarean section found no difference in SSI rates when comparing saline or povidone iodine with no irrigation.<sup>564 565</sup> All three trials used lower volumes of manual irrigation, 300, 100, and 50 mL, respectively.<sup>563–565</sup> Similarly, a recent systematic review that included four RCTs and 1194 patients and compared routine irrigation of abdominal wounds with normal saline with no irrigation prior to wound closure found no difference in SSI rates.<sup>566</sup> An RCT conducted in the emergency room compared tap water with 0.9% sodium chloride irrigation for traumatic wounds prior to soft tissue laceration repair and found no difference in SSI rates.<sup>567</sup>

If irrigation acts to reduce SSI through debridement and washing-away of pathogenic material, it seems that the force or pressure of irrigation at the wound site may influence this benefit.<sup>568 569</sup> An RCT by Hargrove *et al*,<sup>570</sup> including patients undergoing hemiarthroplasty, and an RCT by Nikfarjam *et al*,<sup>571</sup> including patients undergoing major elective, open abdominal operative procedures, both found that powered (pulse)

irrigation with 2 L 0.9% sodium chloride reduced SSI more than low-pressure irrigation of the same solution. However, some evidence shows that high-pressure irrigation (15–35 psi) may weaken the immune response, introduce bacteria into deeper tissues, and cause incisional damage.<sup>568 569</sup>

With the recent FDA ban on bacitracin for off-label injectable use, including irrigation, antibacterial irrigation is becoming scarcer.<sup>572</sup> The clinical popularity of antibiotic solutions for wound irrigation appears to have declined, perhaps due to the association with drug bacteria resistance or other side effects of antibiotics. Although the majority of trials investigating clinical utility appear to have occurred prior to our search criteria (1990 to present), we identified three studies within our search that examined saline and antibiotic irrigation.

Povidone iodine, typically diluted to 0.35%, is the most common antiseptic associated with wound irrigation; however, other antiseptic agents such as 0.04% polyhexanide, a polymer of Serasept 2 solution (Serag-Wiessner, Naila, Germany), have demonstrated potential to decrease SSI rates. Two RCTs in patients undergoing spine surgery found that 0.35% povidone iodine wound irrigation decreased deep and superficial SSI more than 0.9% sodium chloride did.<sup>573 574</sup> Both studies suggested that higher volumes of manual irrigation (2 L), and soaking time of povidone iodine in the wound may be advantageous,<sup>573 574</sup> since a separate trial in children found no benefit with 0.35% povidone iodine in comparison with saline when using 30–60 mL of brief-duration irrigation.<sup>575</sup> Polyhexanide 0.04% has also demonstrated its advantage to reduce SSI over saline irrigation in a recent RCT of elective laparotomies, where the polyhexanide group had fewer SSIs.<sup>576</sup> Al-Shehri *et al* found that ampicillin solution for wound irrigation, in adults and children undergoing appendectomy for acute appendicitis, resulted in fewer SSIs than saline for wound irrigation.<sup>577</sup> Two more recent studies in patients undergoing elective axillary lymph node dissection were inconclusive since there were no SSIs in any of the groups (0.9% saline, gentamicin solution, or clindamycin solution).<sup>578 579</sup>

The UK (NICE) guidelines on SSI advised against using wound irrigation to reduce the risk of SSI; however, these guidelines were based on a literature search in 2008.<sup>1</sup> The WHO guidance from 2016 found insufficient evidence for the use of normal saline wound irrigation, and conditional strength, low quality of evidence for the use of povidone iodine solution, and against the use of antibiotic irrigation.<sup>580</sup> The CDC has recommended against the use of antibiotic irrigation (category IB—strong recommendation; low-quality evidence), but does recommend irrigation with aqueous iodophors (eg, povidone iodine) to prevent SSI.<sup>15</sup> A Cochrane review found no difference between irrigation compared with no intervention; however, it did support the use of pulse irrigation over manual irrigation and antibacterial irrigation (eg, antiseptic and antibiotic) over non-antibacterial irrigation (low-quality evidence).<sup>581</sup> In conclusion, the evidence regarding irrigation to prevent SSIs is conflicting and further well-designed clinical trials are needed.

### Statement

- ▶ *There is insufficient evidence comparing wound irrigation with no intervention to prevent SSI. However, there is unlikely to be harm with saline irrigation. Level of certainty: moderate.*

### Recommendation

- ▶ *Prior to closure and insertion of the spinal cord stimulator implantable pulse generators (IPG)/receivers or intrathecal*

*pump, low pressure wound irrigation with saline through a bulb syringe may be used to remove foreign material debris and blood clots, and to reduce bacterial counts. Evidence: grade C.*

### Skin closure techniques: skin adhesives, staples, and sutures

The presence of sutures alone is thought to increase the risk of bacterial colonization at the incision site and thus increase the risk of SSIs.<sup>582</sup> However, there is also limited information on the best suture material or construction to reduce SSI risk.

Bacterial colonization of sutures creates a biofilm that is difficult for the immune system and antimicrobials to penetrate.<sup>583</sup> Suture types are chosen based on absorbability, tensile strength, as well as risk of associated infections. Sutures can be multifilament or monofilament. Multifilament and natural (silk) sutures are thought to have an increased risk of harboring bacteria between filaments, thus increasing the risk of SSIs.<sup>584</sup> Zucker *et al* performed a meta-analysis evaluating suture types used for abdominal wall closure and found no significant difference in suture type and risk of infection (none of the studies included silk sutures).<sup>585</sup> Triclosan-coated sutures have also been developed and shown to reduce SSIs.<sup>586</sup> However, other studies have not shown any significant difference with use of triclosan-coated sutures.<sup>585 587</sup> A recent systematic review comparing the effect of suture types used for abdominal wall closure on various post-surgical outcomes identified 28 clinical trials involving 10921 participants and 11 types of suture. For the study's predetermined 90% probability threshold, no suture type proved to be the best or superior choice for prevention of SSI, including triclosan-coated sutures.<sup>585</sup> The NICE guidelines recommend the use of antimicrobial triclosan-coated sutures to reduce the risk of SSI, particularly in the pediatric population.<sup>368</sup>

The reduced costs and operative time associated with staples compared to sutures are commonly referenced as the key drivers of staples popularity for skin closure. Dissenters have long voiced that sutures result in improved cosmesis and reduced SSI. Seven RCTs of women undergoing cesarean section or other gynecological procedures (five elective cesarean sections, one emergent cesarean, one benign gynecological procedure) compared infection rates after skin closure with staples or sutures.<sup>588–594</sup> None of these studies found a significant difference in wound infection rates between the suture and staples groups. The low rate of infection may necessitate clinical trials with a larger sample size to be adequately powered.

One RCT (n=11 patients, 22 incisions) with plastic surgeons performing breast reconstruction with tissue expanders found no difference in infection rates between absorbable dermal staples or dermal sutures for closure; however, zero wound infections were noted in both groups during this 6-month period.<sup>595</sup> Wound closure time and cost were significantly reduced with staples while yielding similar cosmetic results.

One RCT (n=50) of patients who underwent extensive surgery in the head and neck area compared skin staples or monofilament sutures for wound closure.<sup>596</sup> Neither group had any infections; however, wound closure time was significantly reduced with staples while yielding similar cosmetic results and costs.

One RCT (n=187) comparing 2-octylcyanoacrylate (2-OCA), subcuticular suture (monocryl), and skin staples for skin closure following THA and TKA, found no significant difference between the groups for either early or late infections, cosmesis, or satisfaction; however, they noted significantly faster wound closure for staples.<sup>597</sup>

A multicenter RCT at 24 institutions conducted between June 1, 2009 and February 28, 2012, of 1800 patients undergoing elective open upper or lower gastrointestinal surgery, compared staples and subcuticular sutures for skin closure.<sup>598</sup> Superficial SSIs occurred in 36 of 558 (6.4%) patients in the sutures group and 36 of 514 (7.0%) patients in the staples group. With lower gastrointestinal surgery, significantly fewer infections occurred in the sutures than in the staples group.

### Adhesives

Cyanoacrylate glue is the most common topical adhesive for skin closure and it typically comes in the form of OCA or butylcyanoacrylate, such as Dermabond (Ethicon, Somerville, New Jersey, USA) or Glubran (GEM, Viareggio, Italy).<sup>599</sup> Adhesives have been used in addition to traditional closure techniques or as a replacement for some of these elements (eg, subcuticular sutures or staples). One prevailing hypothesis is that the topical adhesive forms a barrier over the surgical site to isolate the wound from external pathogens and thus reduce SSI.<sup>600</sup>

Singer *et al* performed a multicenter randomized trial including patients with simple lacerations or surgical incisions closed with OCA versus standard wound closure methods and found no difference in infection rates at 1 week postoperatively.<sup>601</sup> These findings may be limited since the rate of infection in both groups was low, the surgeries heterogeneous with differing closure techniques (traumatic lacerations, excisions of skin lesions or scar revisions, minimally invasive surgeries, and general surgical procedures), and infection assessment occurred over a brief period.

A more recent multicenter RCT including women undergoing cesarean delivery compared tissue adhesive (2-OCA) with sterile strips for skin incision closure and similarly noted no significant differences in wound complications, including infection in 18/238 patients (7.6%), in the tissue adhesive group and 19/241 patients (7.9%) in the sterile strips group.<sup>602</sup> Numerous smaller randomized trials comparing patients undergoing skin closure with adhesives or traditional closure techniques in a variety of surgical specialties have similarly noted no significant difference in the rates of SSI.<sup>603–615</sup>

Two prospective non-randomized cohort studies, one in plastic surgery and the other in spine surgery, observed that skin closure with adhesives reduced SSI in comparison with sutures or staples, respectively.<sup>616 617</sup> The data from the plastic surgery study emphasized that good approximation of the wound edges with underlying sutures was critical to diminishing surface tension and decreasing entry of external contaminants.<sup>616</sup> Of particular relevance to neuromodulation and other surgical pain procedures, the spine surgery data that demonstrated an increased rate of SSI with metal staples was concerning.<sup>617</sup>

Since none of these studies noted increased SSI with topical adhesives, we recommend selectively using topical adhesives for skin closure (in addition to or for replacement of traditional dermal closure) when good approximation of the wound edges is feasible and for patients at higher risk for SSI. A recent Cochrane review stated that sutures were preferred to adhesives with regard to wound dehiscence and that there was no difference in SSI.<sup>618</sup> Likewise, the International Conference on Orthopedic Infections did not recommend topical adhesives because they can be associated with hypersensitivity reactions and do not lower SSI rates in orthopedic procedures.<sup>619</sup> This conclusion was supported by a recent systematic review by Machin *et al*.<sup>599</sup> Although the review only contained three studies, there was no

reduction in SSI; it was implied there was unjustified increased cost.

### Statements

- ▶ *Synthetic, monofilament sutures have the lowest risk of harboring bacteria. This may contribute to a reduced risk of infection. Level of certainty: high.*
- ▶ *For skin closure in wounds at high risk for dehiscence, sutures are better than tissue adhesives for minimizing wound dehiscence. Level of certainty: low.*
- ▶ *Well-approximated wound edges during skin closure may decrease SSI. Level of certainty: moderate.*

### Recommendations

- ▶ *Monofilament sutures should be considered instead of multifilament sutures for superficial skin closure. If the risk of dehiscence is low, monofilament sutures may also be used for deep closure of contaminated wounds and in deep regions considered at high risk for infection. Evidence: grade C.*
- ▶ *The use of sutures or staples for skin closure does not appear to alter infection rates. Evidence: grade C.*
- ▶ *Selective use of tissue adhesives for skin closure, in the presence of optimal skin edge approximation, may be considered, however, it is unclear at present if there is an impact on SSI with the use of tissue adhesives. If wound dehiscence is a concern, sutures would be the first option. Evidence: grade I (insufficient).*
- ▶ *Triclosan-coated sutures can be considered in patients at elevated risk for SSIs. Evidence: grade C.*

### Topical antibiotics and antibiotic-impregnated envelopes for implantable pain therapies

A Cochrane review published in 2016 examining topical antibiotics for preventing SSIs in wound healing by primary intention examined 10 RCTs and four quasi-randomized trials encompassing 6466 participants. The data were inconclusive regarding the effectiveness of different topical antibiotics, mostly due to underpowered comparative studies. Based on this review, topical antibiotics applied to surgical wounds may reduce SSIs compared with no antibiotics. However, limited conclusions could be drawn on adverse events including contact dermatitis and also the impact on development of antibiotic resistance.<sup>620</sup>

In the single RCT, Tarakji *et al* studied 6983 patients who were undergoing cardiac implantable electronic devices (CIED) pocket revision, generator replacement, system upgrade, or initial implantation of a cardiac resynchronization therapy defibrillator (n=3495 antibacterial envelope group and n=3488 control group).<sup>621</sup> The control group received standard-of-care infection-prevention strategies (preprocedural intravenous antibiotics and sterile technique), and the experimental group received an envelope around the generator consisting of multifilament mesh coated with an absorbable polymer mixed with minocycline and rifampin, eluted into the tissue over 7 days. The envelope group demonstrated a 61% reduction in deep-pocket infections over 3 years compared with conventional management with perioperative antibiotics and sterile technique standards of care. A prospective observational study of 1129 patients treated with antimicrobial envelopes for CIED surgery found that the major CIED infection rate in the envelope group was 0.7% compared with an infection rate of 1.0% and 1.3% (p=0.38 and p=0.02) in site-matched and comorbidity-matched control groups, respectively.<sup>622</sup>

The majority of prospective observational studies examining the use of antimicrobial envelopes in CIED surgery found it did reduce the risk of major CIED-related infections.<sup>623–627</sup> One observational study, however, did not result in a statistically significant difference of infection in comparison with control.<sup>628</sup> Ullah *et al* summarized the pooled effect in a systematic review and meta-analysis finding that antimicrobial envelopes in 11 897 patients resulted in a cumulative 66% lower odds ratio of pocket infection.<sup>629</sup> There was a non-significant reduction in mortality in the antibiotic envelope group.

A small retrospective series of 52 patients examining antimicrobial envelopes used to prevent SSIs in SCS implant surgery demonstrated no SSIs at 3 months and no adverse events. Further large-scale studies are needed in the field of neuromodulation.<sup>630</sup>

### Statement

- ▶ *Antimicrobial envelopes provide improved protection against SSI for implantable cardiac devices. Level of certainty: moderate.*

### Recommendation

- ▶ *Consider using antimicrobial envelopes for SCS generator implantation in high-risk patients. Evidence: grade C.*

Table 10 summarizes all of the intraprocedural recommendations.

### Postprocedural recommendations

#### Antimicrobial dressings

A Cochrane review examined 29 trials involving 5718 subjects and evaluated whether SSI risk can be reduced by wound dressings. The systematic review concluded that it is uncertain whether covering wounds healing by primary intention with wound dressings reduced the risk of SSI or whether one type of wound dressing is more effective than others in reducing risk of SSI.<sup>631</sup> There is limited evidence to determine if antimicrobial dressings reduce SSIs for implantable pain therapies.<sup>630</sup> Chlorhexidine-impregnated dressings for percutaneous epidural catheters have been shown to reduce catheter-related colonization.<sup>632</sup>

However, Springer *et al* determined in an RCT with total joint replacement patients that use of an occlusive dressing reduced wound complications (including blistering), reduced dressing changes, and improved patient satisfaction.<sup>633</sup> Although no SSIs were observed in either the standard or occlusive dressing groups, minimizing skin breakdown and complications may decrease risk of SSI. Sharma *et al* reported that wounds managed with occlusive dressings had fewer wound complications and that hydrofiber dressings showed better fluid handling capabilities, but there was no evidence that any dressing reduced SSIs in TJA.<sup>634</sup> Sharma *et al* classified dressings into passive (gauze, absorbent pads), active (films, hydrocolloid, hydrofiber), and interactive (antimicrobial, biomaterial, vacuum dressings). In 12 RCT studies, eight had SSI data but no dressing type was found to be superior to another in terms of reducing SSI.<sup>634</sup>

Two interactive dressings have recently been studied: Aquacel AG (hydrofiber) and Silverlon surgical dressing (woven nylon dressing with silver plated matrix and waterproof foam adhesive). In the study by Cai *et al*, 903 patients treated with Aquacel were compared with patients treated with standard xeroform and gauze.<sup>635</sup> Aquacel was found to be an independent risk-reduction factor with regard to SSI. This was also confirmed by Grosso *et al* who compared almost 600 subjects per group and demonstrated Aquacel benefit. In each study, dressings were removed at day 2.<sup>636</sup> Additionally, Tisosky *et al* found, in a study of >300 subjects with Silverlon dressing applied for 7

**Table 10** Intraoperative recommendations for reducing SSIs

Recommendations	USPSTF grade*	Recommendations based on procedure type†				Comments
		A	B	C	D	
Chlorhexidine-based products are the preferred skin antiseptic in surgical and interventional pain procedures (including neuraxial).	B	√	√	√	√	In individuals with chlorhexidine reactions or allergies, povidone iodine combined with alcohol solution should be considered.
Sterile gloves.	B	√	√	√	√	
Personal protective equipment (surgical cap and eye protection).	B		√	√	√	Proceduralists should always wear surgical cap and mask when performing procedures in an OR setting.
Sterile surgical gown.	B			√	√	
The rubber septum on medication vials should be disinfected with alcohol prior to piercing.	B	√	√	√	√	
Use of a stylet needle is recommended when performing intradiscal procedures.	B			√		
A double-needle technique for performing intradiscal procedures is recommended.	B			√		
Sterile C-arm cover.	B			√	√	
Avoid contact with the C-arm	B	√	√	√	√	
Operating rooms should have HEPA filtration systems.	B			√	√	
Maintain operating room humidity levels between 20% and 70%.	B			√	√	
Avoid unnecessary delays that result in increased procedure duration.	A			√	√	
Minimize OR traffic.	C			√	√	
Outer glove change by the surgeon and surgical staff following draping and prior to incision.	C			√	√	
Outer glove change before implantable device handling.	C				√	
Low-pressure wound irrigation with saline through a bulb syringe.	C				√	
Monofilament rather than multifilament sutures should be considered for superficial skin closure.	C				√	
Consider using antimicrobial envelopes for SCS generator implants in high-risk patients.	C				√	
Triclosan-coated sutures can be considered in patients at elevated risk for SSIs.	C				√	
Application of vancomycin powder to the surgical wound is not routinely recommended.	I				√	
Full-length patient surgical body drape.	B			√	√	
Limit tissue trauma, maintain hemostasis, eradicate dead space, and avoid the electrocautery at tissue surface.	B				√	

\*Grades are described in table 1. A represents the highest level evidence and I (insufficient) the lowest.

†Procedures are classified in table 3.

HEPA, high-efficiency particulate air; OR, operating room; SCS, spinal cord stimulation; SSI, surgical site infection; USPSTF, US Preventative Services Task Force.

days compared with >500 subjects with xeroform and gauze for 2 days, that the infection rate was halved (8.4% control; 3.9% Silverlon) with the use of the Silverlon dressing.<sup>637</sup>

Most recently, 22 studies involving >5400 participants evaluated the effectiveness of antimicrobial dressings in reducing SSIs.<sup>638</sup> In this study Jiang *et al* determined that vitamin E silicone-containing dressings and mupirocin dressing were effective at preventing SSIs while dialkylcarbamoyl-chloride-containing dressings were less effective. It remains to be determined if these novel products improve outcomes, and further study is required before recommendations can be made, however, consideration of use in high-risk individuals could be beneficial.

The CDC has recommended (CDC category IB; recommendation, strongly recommended for implementation supported by some experimental, clinical, or epidemiological studies and strong theoretical rationale) occlusive sterile dressing for 24–48 hours postoperatively to reduce the risk of SSI.<sup>29</sup> In addition, NACC has also recommended applying occlusive dressing following SCS trials and implants.<sup>150</sup>

#### Statements

- *There is limited evidence to determine if antimicrobial dressings reduce SSIs for implantable pain therapies. Level of certainty: high.*

- *Chlorhexidine-impregnated dressings for percutaneous epidural catheters have been shown to reduce catheter-related colonization. Level of certainty: moderate.*

#### Recommendations

- *Antimicrobial dressings could be considered in high-risk patients undergoing implantable pain device surgery. Evidence: grade C.*
- *Chlorhexidine-impregnated sponges may be considered for any procedure involving a percutaneous indwelling catheter or stimulator leads in high-risk individuals. Evidence: grade C.*
- *The use of bio-occlusive dressings is recommended for a minimum of 24 hours after surgery for implantable pain therapies. Evidence: grade B.*

#### Postoperative antibiotics for implantable pain therapies

The continuation of antibiotics in the postoperative period is not recommended beyond 24 hours for clean surgical wounds. Prolonged antibiotic use in the postoperative period does not improve outcomes and may result in poorer outcomes. Ohtori *et al* retrospectively reviewed patients that had 2 g of intravenous cefotiam given for 2 days vs 7 days after lumbar spine surgery

and found that, although there was no difference in rate of SSIs, the group that received 7 days of intravenous antibiotics had a significantly greater length of hospital stay, time until regaining normal body temperature, and CRP level.<sup>639</sup> The SCIP guidelines also recommend discontinuation of antibiotics within 24 hours of surgery.<sup>361</sup>

NACC recommended that postoperative antibiotics be limited to the first 24 hours following routine procedures and that clinician discretion be used concerning continuation of antibiotics in higher-risk individuals.<sup>150</sup> In addition, SCIP recommends discontinuing antibiotics within 24 hours of surgery.<sup>361 640</sup> A recent large-scale meta-analysis confirms the position that there is no incremental benefit in continuing antibiotics into the post-procedure period when best practice standards are followed.<sup>641</sup> This was based on 52 RCTs with 19 273 participants. Interestingly, in this analysis the only studies to demonstrate a relative risk reduction in SSI with extension of antibiotic treatment beyond surgery were those who did not adhere to best practice standards for surgical antibiotic prophylaxis (identified as (1) timing of first preoperative antibiotic dose within 60 min before incision and (2) repeat antibiotic administration if procedure duration exceeds two times of the antibiotic's half-life), including studies performed prior to such clear guidelines being available. No benefit of postoperative antibiotic continuation was identified when surgical antibiotic prophylaxis best practices were adhered to. Taken together, these data do not find incremental benefit in continuing antibiotics into the postoperative period.

Use of vancomycin powder in the surgical bed continues to be a matter of much debate within the neurosurgical and orthopedic literature. Animal studies have suggested that local vancomycin is effective and more potent at reducing SSIs with implantable therapies than systemic vancomycin.<sup>642</sup> However, human data are mixed. The most recent NACC guidelines suggested that there is inconclusive evidence to recommend the practice but that it could potentially be beneficial in select cases.<sup>150</sup> Since that time multiple small studies have been published with conflicting findings regarding the effectiveness of vancomycin powder in preventing SSIs when applied during spine surgery, joint arthroplasty, and foot and ankle surgeries.<sup>643–645</sup> A recent meta-analysis by Peng *et al* recommends topical application of vancomycin in joint arthroplasty.<sup>646</sup> Additionally, another recent meta-analysis suggested that intrawound application of vancomycin may increase Gram-negative and polymicrobial SSIs and that this practice should be restricted to use in only the most high-risk patients.<sup>647</sup>

#### Statements

- ▶ *Prolonged antibiotic use in other surgical subspecialties has not been shown to improve outcomes. Level of certainty: high.*
- ▶ *The application of powder vancomycin to the surgical wound bed is not FDA approved and additional studies are needed for safety and efficacy prior to supporting the routine use of vancomycin powder for implantable pain therapies. Level of certainty: low.*

#### Recommendations

- ▶ *Antibiotics should not be continued beyond 24 hours for implantable pain therapy cases. Evidence: grade D.*
- ▶ *Application of vancomycin powder to the surgical wound is not routinely recommended. Evidence: grade I (insufficient).*

## Diagnosis and treatment of pain procedural infections

### CNS infections

The clinical spectrum of central neuraxial infections following neuraxial anesthesia or pain interventions can manifest as the well-known complications of epidural abscess or meningitis, but less common manifestations such as spinal abscess, discitis, paraspinal or psoas abscess, CSF fistula, or even necrotizing fasciitis have been well documented.

The classic symptom of epidural abscess is the triad of fever, localized back pain, and sensory/motor deficits, but these symptoms do not always present together and pain may present as the sole symptom without neurological deficit.<sup>648</sup> A review of symptomatology by Bos *et al* showed that a significant proportion of patients mainly had fever, while the second most common symptom was pain or spinal tenderness, which at times was the only presenting symptom.<sup>648</sup> The triad of symptoms was present in only 34% of patients. There can be a significant time gap since the antecedent neuraxial anesthesia and the development of epidural abscesses, and a majority of the epidural abscesses may develop after the discontinuation of the epidural catheters. The presence of sensory or motor deficits is a poor prognostic sign and patients with epidural abscesses without focal neurological deficits usually have a good recovery; abscesses at the lumbar levels have better prognosis compared with abscesses in the thoracic levels.

The classic symptoms of meningitis (high fever, headache, and nuchal rigidity) are seldom found in patients suffering from meningitis secondary to neuraxial anesthesia. Hence, similar to epidural abscess, clinicians need to have a high degree of suspicion.<sup>48 50 51</sup> Meningitis following neuraxial anesthesia has a shorter time gap between the procedure and the development of symptoms, but can still have a delayed manifestation well beyond the duration of hospital stay. Meningitis usually has excellent prognosis with antibiotic therapy unless focal neurological symptoms are present.

### Statements

- ▶ *The classic presentation of epidural abscess (triad of spine tenderness, fever with chills, and neurological deficits) or meningitis (triad of photophobia/headache, fever, and neck rigidity) is seldom present in patients developing these complications following neuraxial anesthesia. Fever with spine tenderness (epidural abscess) or fever with headache/photophobia (meningitis) are the common presenting symptoms. Level of certainty: moderate.*
- ▶ *Epidural abscess or meningitis following neuraxial anesthesia is rare and may have a variable onset and progression. Level of certainty: moderate.*
- ▶ *Neurological recovery following CNS infections is dependent on the severity of the disease and the time interval between onset and treatment. Level of certainty: moderate.*

### CNS infections: diagnostic tests

The most common and most sensitive method of detection for epidural abscess is MRI, although other modalities such as CT scan or myelography have been performed.<sup>45–52 158 183 187 192 197–199</sup> Rosero and Joshi<sup>185</sup> estimated that the need for MRI without the need for any additional interventions following neuraxial anesthesia is approximately 9.1 MRI scans per 100 000 central neuraxial blocks.

Meningitis is classically diagnosed clinically with confirmation following CSF analysis and culture of the organism. Other methods of identifying the microorganism in the CSF include

PCR and interferon gamma-release assays.<sup>45–52 186 187 189 192 195–199</sup> Meningitis has also been diagnosed using MRI, as the contrast-enhanced MRI has been shown to identify the presence and extent of meningeal inflammation. However, given that the sensitivity and specificity of the various MRI modalities differ, CSF analysis still remains the gold standard for diagnosis.<sup>649</sup> All institutions performing neuraxial anesthesia should have a policy to order MRI at the earliest time after a suspicion of an epidural abscess. A policy for subsequent referral to the nearest neurosurgical facility and a ‘scan and then ask questions’ approach is probably in the best interest of patient safety.

#### Statements

- ▶ *The most common and most sensitive method of detection for epidural abscess is MRI. Level of certainty: high.*
- ▶ *In patients with meningeal signs, a CSF analysis with culture confirms the presence of meningitis. Level of certainty: high.*

#### Recommendations

- ▶ *Suspicion of epidural abscess, especially in patients with systemic symptoms or sensorimotor deficits following neuraxial anesthesia should be investigated at the earliest opportunity with an MRI scan followed by urgent neurosurgery and infectious disease consultations. If MRI is not available or contraindicated, CT imaging should be considered. Evidence: grade A.*
- ▶ *CSF analysis (if not contraindicated) is the diagnostic method of choice for suspected meningitis. Evidence: grade A.*

#### Treatment of infectious complications following neuraxial blocks

Superficial infections most often require conservative management and antibiotic therapy. Incision and drainage are often required in patients with deep-seated infections, systemic symptoms (fever, chills, raised CRP, and/or ESR) or infections resistant to conservative measures. Almost all cases of meningitis and most cases of epidural abscesses have good recovery unless there are focal neurological deficits. Bacterial meningitis and epidural abscesses often require prolonged antibiotic therapy and are associated with prolonged hospitalization. While immediate surgical decompression is usually recommended for treating epidural abscesses on identification, conservative management has been effective in some cases.<sup>46 47 49–51 158 183 187 192 648</sup> Urgent surgical decompression or percutaneous drainage for epidural abscesses is usually needed if there is rapid progression of symptoms, any sign of spinal cord or thecal sac compression (especially motor deficits or cauda equina syndrome), or if neurological or systemic symptoms do not respond to antibiotic therapy.<sup>46–53 197 198</sup> Otherwise, slowly developing or incidentally detected abscesses can initially be treated conservatively with antibiotic therapy in hopes of dissipation or resolution of symptoms within the first 48 hours of therapy. Non-operative management has also been chosen in cases where the patient declines surgical options or medical comorbidities impede surgical intervention.<sup>648</sup>

#### Outcomes of infectious complications following neuraxial blocks

Most superficial infections respond to conservative management and, even if surgical drainage is needed, skin and superficial infections usually have a good prognosis and complete recovery. While resolution of infection with antibiotic therapy is often possible with superficial and deep infections, resolution often requires hospitalization. Also, prolonged antibiotic therapy for

deep-seated infections may increase the risk of adverse events, primarily related to the gastrointestinal tract.<sup>650</sup>

Recovery from spinal/epidural abscesses depends on the degree and duration of thecal compression,<sup>51</sup> location of the abscess (lumbar abscesses tend to have a better prognosis compared with cervical or thoracic abscesses due to less thecal compression),<sup>52</sup> and whether neurological symptoms exist at presentation. Those patients with motor deficits or cauda equina signs and symptoms at presentation tend to have incomplete recovery.<sup>50–52 648</sup> Some patients with meningitis respond to treatment and make complete recovery, but neurological sequelae are not uncommon and the risk of mortality following neuraxial block-related meningitis is between 13.3% (for epidural-associated meningitis) and 15.3% (for spinal-associated meningitis).<sup>54</sup>

#### Statement

- ▶ *Early detection of a spinal/epidural abscess is critical since the neurological recovery depends on the degree and duration of thecal compression and the degree of neurological symptoms at presentation. Level of certainty: high.*

#### Recommendations

- ▶ *Catheter use should be discontinued at the earliest signs of infection followed by appropriate early medical/surgical management. Evidence: grade A.*
- ▶ *The decision to perform single-injection regional nerve blocks in patients with localized well-controlled infections should be decided on a case-by-case basis if these blocks are not performed near the infected site. The safety of continuous catheters in such patients is unknown and, hence, not preferred. Evidence: grade I (insufficient).*

#### Presentation and identification of implantable pain device infection

In addition to healthcare costs, associated patient morbidity, mortality, and the loss of a functioning device have a significant impact on patients' experience and quality of life. Appropriate counseling to patients regarding signs of infection and prompt recognition and investigation of these symptoms is essential for any practice offering implantable device therapies for treatment of chronic pain.

Infection of an implanted device can manifest with or without systemic signs of infection such as pain, malaise, or fever. The presentation of swelling, erythema, tenderness, erosion, or drainage at the site of an implanted device (at the IPG pocket), tunneling site, or at the midline incision for anchoring should raise concern for possible infection and prompt further investigation. Infections involving the neuroaxis including epidural abscess, meningitis, and/or discitis/osteomyelitis are considered complicated and often require interdisciplinary management with infectious disease experts and possibly neurosurgeons or orthopedic surgeons.<sup>150</sup>

One multisite retrospective study involving 2737 implanted SCS devices identified SCS-related infection in 2.45% of cases (n=67), with 2.27% occurring within the first year following implant.<sup>651</sup> The most common presenting signs and symptoms included pain (75.4%), erythema (63.1%), drainage (49.2%), swelling (30.8%), fever (26.2%), wound dehiscence (21.5%), and nausea (4.0%). Interestingly, although most patients presented with pain, some other classic signs of infection including erythema, swelling, drainage, and fever were not reliably present in patients with SCS-related infection. Further evaluation commonly included laboratory investigation, with WBC counts

and inflammatory markers (ESR and CRP). More than 45% of confirmed cases of SCS infection had an elevated WBC count ( $>11.0 \times 10^9/L$ ), nearly 45% had elevated ESR ( $>29$  mm/hour, mean 51.2 mm/hour), and 53.3% had elevated CRP ( $>4.0$  mg/L, mean 38.2 mg/L). Most patients did not require imaging for further evaluation, but when performed imaging included CT (27.7%), ultrasound (6.4%), MRI (2.1%), and abdominal radiographs (2.1%). One-third of imaging studies were normal, 3/18 had IPG pocket abscesses, 4/18 had anchoring site abscesses, and 1/18 had evidence of osteomyelitis/discitis. Nearly 90% of cases of infection reported culture results, with 76.4% ( $n=42$ ) demonstrating positive culture. Among positive culture results, 85.7% (36/42) were obtained from the IPG pocket site, 28.6% (12/42) from the anchoring site, 11.9% (5/42) from the lead tip, and 4.8% (2/42) from blood cultures. The most commonly cultured organism was *S. aureus* (83.3%, 35/42) followed by *P. aeruginosa* (4.8%, 2/42), *Streptococcus* spp (2.4%, 1/42), *S. marcescens* (2.4%, 1/42), and mixed flora (4.8%, 2/42). Most cases (64/67) were treated with antibiotics including oral and intravenous antibiotics (40.3%, 27/64), oral antibiotics only (28.4%, 19/64), and intravenous antibiotics only (26.9%, 18/64). Twelve cases were treated with surgical incision and drainage, and 77.6% (52/67) ultimately required system explantation. Three of these patients required additional intervention for pocket-site infection, including one patient who required a flap procedure performed by a plastic surgeon. Fourteen of the explanted cases were followed up by MRI, and among these an epidural abscess was discovered in three patients. Fifteen patients were able to have their SCS systems salvaged, including 13.4% ( $n=9$ ) with antibiotics only, and 9% ( $n=6$ ) with incision and drainage.

Despite concerns for elevated infection risk in patients with cancer due to underlying comorbidities including leukopenia and malnutrition, a retrospective review of 217 patients with cancer who underwent IDD implant for cancer-associated pain found a relatively low infection rate of 0.9% ( $n=2$ ) within the first 6 months.<sup>297</sup> Most patients (79.3%,  $n=172$ ) were on some form of antineoplastic therapy within 30 days prior to implant, including chemotherapy (46.5%,  $n=101$ ), immunotherapy (28.6%,  $n=62$ ), radiation (28.1%,  $n=61$ ), and corticosteroids (32.3%,  $n=70$ ). One patient with infection presented 4 days after implant with fever, malaise, erythema at the pocket site, and pancytopenia. The device was explanted, with culture from the pocket site positive for MSSA, and the patient was treated with intravenous antibiotics with resolution of infection. The second patient presented with erythema, tenderness and drainage from the pocket and lumbar sites 34 days after implant; the device was explanted and cultures from the pocket site were positive for MSSA. The patient was treated with 2 weeks of antibiotics and recovered without recurrence of infection.

Another retrospective review of 64 patients treated with an implantable IDD device for cancer-associated pain found a higher risk of infection at 6.2% (4/64).<sup>652</sup> Three patients had developed pocket-site infections, and one case was associated with meningitis. The patient who developed meningitis had received chemotherapy, systemic corticosteroids, and radiotherapy within 90 days prior to implant, as had several other patients in the studied cohort.

In a retrospective review of 145 patients implanted with IDD for chronic pain (including malignancy and non-malignancy-related indications), 19 patients (8.71%) developed infections, 14 of which were related to the implanted device.<sup>653</sup> Eight of these 14 patients underwent system removal with or without antibiotic therapy, and the remaining were treated with antibiotics alone. Five patients were diagnosed with meningitis, all of

whom underwent explantation of the pump and catheter. One patient with meningitis and urinary tract infection ultimately died of septic shock. Presenting signs and symptoms of meningitis included fever, headache, nausea, and a systemic inflammatory response, and all patients with meningitis were also found to have pocket-site infection. Patients with meningeal infection were treated empirically with broad-spectrum antibiotics with activity against *Pseudomonas* and *Staphylococcus* for up to 3 weeks. Device-related infection was most likely to occur within 3 months after implant, catheter exchange, or pump refill.

Clinical presentation may vary according to the timing of infection following implant. Acute infections (typically presenting within 4–6 weeks) generally manifest with fever, local inflammation, and possibly foul-smelling discharge from the implant site. Most neuromodulation-related SSIs occur within the first 90 days, and any deep infection occurring at the surgical site within the first 90 days following implantation<sup>5,27</sup> is defined as a device-related SSI.<sup>11 145–149 654 655</sup> Chronic infections may present months later with localized signs of inflammation and occasionally with discharge and signs of wound dehiscence. Chronic infections presenting with a mature biofilm are far less likely to be salvageable and will usually require full system explantation.<sup>656</sup>

The evaluation of a patient with suspected infection of an implanted device should always begin with a thorough history and targeted physical examination. Laboratory investigation may include CBC with differential, and inflammatory markers (ESR and CRP). Blood cultures should be obtained if the patient is septic. WBC, ESR, and CRP rise transiently in the postoperative period due to the body's acute stress response, and acute SSI must be differentiated clinically from postsurgical inflammation. Patients with underlying cancer or rheumatological diseases will also have elevated baseline inflammatory markers.

CRP is considered in the surgical literature to be superior to ESR in the diagnosis of SSI in the acute postoperative period due to its more reliable peak and return to baseline, although depending on the extent of surgical intervention CRP may be elevated as an inflammatory response in the absence of infection. In evaluation of the WBC count, it is helpful to assess overall WBC count, neutrophil percentage, and lymphocyte percentage. Neutrophil count and percentage both attain their peak value 1 day postoperatively, and elevations of these values at or beyond postoperative day 4 may reliably predict infection. CRP reaches its peak on postoperative day 4, and comparing CRP elevation on postoperative day 7 with postoperative day 4 may reliably predict SSI.<sup>657</sup> CRP returns to baseline within 2–3 weeks following surgery, while ESR remains elevated for a longer, although more variable, period of time. Thus, a normal CRP is a more reassuring marker for absence of infection than ESR, and similarly more sensitive in the detection of SSI.<sup>150</sup> Made by the liver in response to tissue damage, malignancy, inflammation, or infection, CRP is characterized by rapid and predictable response to an inciting event and returns to baseline more rapidly than ESR, which is an indirect measure related to blood albumin and globulin and can remain elevated up to 1 year following major surgery.<sup>658</sup> Elevated CRP beyond 7 days postimplant should raise concern for device-related SSI.

Diagnostic imaging is indicated if there are signs of neuraxial spread. MRI with and without contrast is the optimal study, but in patients who cannot undergo MRI, a CT scan can be performed. If symptoms concerning for a more complicated process such as meningitis, osteomyelitis/discitis, and/or epidural abscess are present, appropriate diagnostic investigation and surgical management are required.

### Appropriate culture technique and methods for culturing infections associated with implantable devices (both surgically and in the office)

Intraoperative culture technique for implantable devices should include the use of sterile instruments (sterile swab) transferred directly to the culture container and delivered for analysis in a timely fashion to reduce the risk of contamination.<sup>659</sup> Tissue culture has been found to be superior to swab culture in the diagnosis of device-associated infection.<sup>660</sup> Following removal of the IPG or IDD reservoir from the pocket, the specimen should be obtained from the deep portion of the pocket, preferably multiple swabs from distinct deep areas of the pocket site. A sample of the fibrotic capsule may also be excised and transferred to a sterile container for evaluation and processing. There are high reported rates of negative culture results in cases of suspected SSI, and negative culture results should not be solely used to rule out infection.<sup>651 661</sup> In addition, the initiation of antibiotics prior to obtaining tissue cultures may lead to a negative culture result. However, positive culture results may aid in the selection and duration of antimicrobial therapy.

### Management of infected pain device implants

In case of a suspected superficial infection or cellulitis, attempted salvage with antibiotics and frequent wound checks may be appropriate. In the case of a suspected deep SSI, consideration of irrigation and debridement with antibiotics and attempted salvage may be appropriate, but explantation of the entire device is more prudent and often necessary. In addition, cultures should be obtained from both the IPG pocket and midline incision sites and sent for Gram stain and bacterial cultures. Routine testing of mycobacteria or fungi is not recommended.<sup>662</sup> Ideally, surgical cultures would be obtained prior to the initiation of antibiotics if possible.

### Management of perioperative fever

Any patient presenting with fever following SCS implant or trial or IDD implant should undergo urgent evaluation for possible device-related SSI. This should include emergent clinical evaluation with complete history, physical examination including neurological examination, and inspection of the incision sites, laboratory evaluation including blood cultures, WBC count, CRP, and ESR, and consideration of imaging based on clinical presentation. If there is a concern for sepsis or meningitis, hospital admission is indicated and commencement of empiric broad-spectrum antibiotics with activity against staphylococci, CoNS, and antimicrobials with activity against MRSA if risk factors are present. In the case of hemodynamic instability or symptoms of sepsis, treatment should not be delayed in favor of obtaining intraoperative cultures. If deep SSI is suspected, the patient should be brought to the OR promptly for system explantation with irrigation and debridement.<sup>150 662</sup>

### CHALLENGES OF TREATING INFECTIONS ASSOCIATED WITH IMPLANTABLE DEVICES

Infections associated with implantable devices most commonly occur at the generator site (54%).<sup>663</sup> These infections pose specific challenges due to the formation of biofilm around implanted devices that is poorly penetrated by antibiotics and inhibits antimicrobial activity. In a large nationwide database examining the outcomes of patients with chronic pain spinal implantable electronic devices, complications from infection

were higher among patients who did not undergo device removal in the presence of SSI.<sup>8</sup>

Implant-associated deep SSI thus often requires explantation of the system as well as debridement of any surrounding necrotic and fibrous tissue for adequate source control. Biofilm may be thought of as microbial colonies embedded within an adherent matrix.<sup>664</sup> Bacteria first adhere to a surface (in this case, an implanted device) mediated by bacterial surface proteins. Mature biofilm involves the production of an extracellular matrix in which bacteria become embedded, ensuring cell-to-cell adhesion of proliferating cells. The biofilm is resistant to antimicrobial penetration and allows the spread of resistance to antibiotics via gene exchange, which facilitates the development of highly virulent strains of bacteria.

IDD systems pose specific challenges in terms of the treated patient population (increased comorbidities in patients with malignancy, compromised nutritional status, or mobility challenges in patients receiving intrathecal baclofen), as well as the fact that the catheter tip resides in the intrathecal space. In terms of infectious risk, there is increased concern for CSF involvement when an infection is suspected. Infectious complications including intracranial abscess have been reported with implanted IDD systems.<sup>665</sup> Thorough investigation of any new neurological changes, including CSF examination and advanced imaging of the neuroaxis, may be necessary depending on the presentation. Normal CSF examination does not necessarily exclude CNS involvement; therefore, device explantation is often required, particularly in cases of deep SCS infection.<sup>666</sup> IDD systems delivering IT baclofen complicated by infection pose considerable management challenges due to the danger of acute baclofen withdrawal in the case of system explantation. Baclofen withdrawal can be life-threatening. The suggested treatment for intrathecal baclofen withdrawal is the restoration of intrathecal baclofen at or near the same dosage as soon as possible. Replacement with oral baclofen and sometimes intravenous benzodiazepines is necessary in the case of device removal without immediate device replacement. However, oral baclofen should not be relied on solely to halt the progression of intrathecal baclofen withdrawal. In a retrospective review of 294 pediatric patients with cerebral palsy undergoing IDD implant with baclofen, 28 developed infections.<sup>667</sup> Eight patients underwent immediate reimplantation, five underwent reimplantation in a second procedure, two patients were re-implanted following the placement of bone cement spacers, three patients required multiple wash-out procedures to clear the infection, and eight patients decided against reimplantation. Another retrospective review of implanted intrathecal baclofen drug delivery systems in a pediatric population found that most patients (59%) required explantation, particularly in cases of deep infection or infections involving organ space.<sup>668</sup>

### Intraoperative and postoperative wound management recommendations for device explant procedures

In the case of infection, it is recommended to create a new incision over the pocket to remove infected hardware and debride all necrotic and fibrotic tissue including the capsule, followed by extensive irrigation. It is important to achieve adequate hemostasis to avoid hematoma development. Although removal of the fibrous capsule surrounding an infected IPG or IDD pump is sometimes recommended for source control, one RCT evaluating the effect of pocket capsule decortication in the routine revision

of cardiac implantable device generators found increased risk of hematoma formation in the pocket revision group without benefit in terms of reduced infection risk.<sup>669</sup> However, given that there was no incidence of infection in either group and the overall low incidence of device-related SSI, a larger sample size might be needed to rigorously study this question.

High-quality evidence to recommend specific wound bed treatments in the management of device-related SSI is lacking.<sup>581</sup> Various recommendations are made in the neurosurgical literature related to superficial and deep infections following instrumented fusion. High-volume, low-pressure irrigation with normal saline following debridement of necrotic tissue is certainly recommended; however, the use of other solutions such as povidone iodine, antiseptic solutions, and antimicrobial solutions are often employed.<sup>670 671</sup>

There is limited evidence to support the use of intraoperative wound bed treatment with vancomycin powder in patients undergoing explant for infection.<sup>672</sup> The use of vancomycin powder may be most helpful in deep SSI related to instrumented spine surgery.<sup>673</sup> Commercial products such as an antibacterial envelope eluting minocycline and rifampin may reduce SSI but are costly, and are often not routinely employed in most neuromodulation practices, but may be considered in high-risk patients such as those undergoing reimplantation following previous SSI.<sup>674</sup>

There is currently no clear evidence to support the use of delayed primary closure or secondary closure in the case of neuromodulation-related SSI. There is also no clear evidence to support a specific type of suture material in infection-related device explant procedures.

In patients with known deep device-related SSI and systemic infection requiring hospitalization, consideration can be given to placement of a drain or wick for a short period of time (typically for a percutaneous device this would not be required beyond 24 hours) to aid in further drainage after skin closure.

Adjunctive therapies for treatment of SCS-related and IDD-related infections with limited evidence include hyperbaric oxygen therapy (HBOT), which was employed alongside antibiotic therapy in 14 instances of neuromodulation hardware-related SSI, 12 of which were salvaged without explantation.<sup>675</sup> There was one reported malfunction of an IDD system treated with HBOT, raising safety concerns. HBOT as an adjunctive treatment for SSI warrants further study.

### Antibiotic treatment for implantable pain device infections

The causative organisms of most SSI originate from skin flora, most typically *S. aureus*, CoNS, *E. coli*, and *Pseudomonas*. Antibiotic therapy should be directed by culture result whenever possible, but due to the rise of resistant strains of bacteria, empiric coverage should include agents against suspected MRSA if the patient has relevant risk factors.<sup>676</sup>

An approach to the management of SCS device-related SSI is based on limited evidence from studies specific to neuromodulation devices, as well as literature from related disciplines and CDC guidelines.<sup>662</sup> In the case of suspected superficial SSI, a trial of oral antibiotics may be considered. This is typically offered for 7–10 days and should include an agent with activity against staphylococcal and streptococcal species, such as a first-generation cephalosporin. For patients with risk factors for MRSA, an agent with MRSA coverage should be incorporated. A superficial abscess may require incision and drainage.

Deep SSI will require surgical incision and drainage and usually device explant. Clinically stable patients with localized infection

may undergo intraoperative culture prior to commencement of empiric antibiotic treatment, but treatment should not be held for patients with severe signs of sepsis such as hemodynamic instability. Cases of deep SSI typically require explantation of the device. For uncomplicated cases of deep SSI with negative blood cultures and device explant, a course of 7–10 days of antibiotic therapy is usually sufficient for source control,<sup>662</sup> although a longer duration of therapy may be required.<sup>656</sup>

### Infectious disease consultation

Collaboration with an infectious disease specialist is recommended in certain cases of implanted device-related SSI, particularly in complicated cases of deep SSI. Consultation may be considered for patients with pertinent drug allergies or sensitivities, patients with chronic kidney disease, and/or patients with comorbidities putting them at elevated risk for infection, such as patients with cancer undergoing immunosuppressive treatment or patients with diabetes mellitus, obesity, and/or nicotine use. For patients with deep SSI complicated by sepsis, meningitis, osteomyelitis/discitis, or epidural abscess, partnership with infectious disease colleagues is imperative. Consultation with an infectious disease specialist is recommended in cases of suspected involvement of neuraxial structures.<sup>150</sup> If explantation is delayed due to patient-specific factors, such as the need to hold antithrombotic medications, consulting an infectious disease specialist may be beneficial for guidance on antibiotic therapy recommendations.

### Recommendations for reimplantation of implantable pain devices following SSI

Patients previously undergoing explantation for SSI should be carefully re-evaluated to consider whether they remain candidates for implantable device therapy. Modifiable risk factors that may have contributed to the development of SSI must be optimized prior to consideration of reimplantation. Level I evidence does not exist to guide decision-making with respect to optimal timing of reimplantation.<sup>677</sup> Expert guidance regarding timing for reimplantation in the case of uncomplicated infection has been suggested to be 12 weeks.<sup>678</sup> Extrapolating from recommendations for implanted cardiac devices, some practitioners recommend placing the new IPG device contralateral to the original side.<sup>679</sup>

Data are insufficient to suggest that monitoring trends of inflammatory markers following infection improves outcomes. However, marker trends may be helpful in the event of recurrent signs or symptoms or if reimplantation is being considered. CRP will return to baseline within 3 weeks of resolved infection, but ESR may remain elevated for a prolonged period (up to 1 year).

### Statements

- *Signs and symptoms of an SSI include (1) pain, malaise, and/or fever and/or (2) swelling, erythema, tenderness, or drainage at the pocket site, tunneling site, or midline incision in the case of implantable pain devices. However, many patients do not present with all the classic signs and/or symptoms of infection. Level of certainty: high.*
- *Mortality is higher in patients with chronic spinal pain implantable devices hospitalized for SSI who are treated with antibiotics compared with those undergoing complete system explant. Level of certainty: moderate.*
- *Evidence is lacking to recommend specific wound bed treatments in the management of implantable pain device-related infection. Level of certainty: high.*

**Table 11** Postprocedural recommendations for reducing SSIs

Recommendations	USPSTF grade*	Recommendations based on procedure type†			
		A	B	C	D
Antibiotics should not be continued beyond 24 hours for implantable pain therapy cases.	D			✓	✓
Antimicrobial dressings could be considered in high-risk patients.	C				✓
Use of bio-occlusive dressings for a minimum of 24 hours.	B				✓
Suspicion of epidural abscess should be investigated at the earliest opportunity with an MRI scan followed by immediate neurosurgery and infectious disease consultation. If MRI imaging is not available or contraindicated, CT imaging should be considered.	A		✓	✓	✓
CSF analysis (if not contraindicated) is the diagnostic method of choice for suspected meningitis.	A		✓	✓	✓
Indwelling catheter use should be discontinued at the earliest signs of infection followed by appropriate early medical/surgical management.	A		✓	✓	
Complete blood count with differential, erythrocyte sedimentation rate, and C reactive protein should be obtained and monitored for trends when SSI is suspected.	A	✓	✓	✓	✓
In the case of SSI requiring surgical debridement, irrigation, revision, or explantation, intraoperative cultures should be obtained, ideally including tissue and prior to initiation of antibiotics, to guide selection of antibiotic therapy.	A				✓
Complete system explantation should be considered in cases of device-related SSI, particularly for deep (subfascial) and/or complicated device-related SSI.	A			✓	✓
Antibiotic therapy should be guided by preoperative or intraoperative culture results when possible.	A	✓	✓	✓	✓
A trial of oral antibiotics may be considered in cases of superficial SSI with close clinical monitoring. This is typically offered for 7–10 days and should include an agent with activity against staphylococcal and streptococcal species.	C	✓	✓	✓	✓
An antibiotic therapy plan should be developed with the help of an infectious disease specialist in cases of complicated SSI (including any involvement of neuraxial structures), systemic infection, multidrug-resistant infection, or for patients with pertinent medication allergies, chronic kidney disease, and/or with comorbidities placing them at elevated risk for resistant infection.	B	✓	✓	✓	✓
Consider consultation with an infectious disease specialist if reimplantation is being considered.	A				✓
A minimum 12-week interval is recommended prior to reimplantation in appropriate candidates following explantation for a device-related infection. Reimplantation at a site not involved in SSI should be considered.	C				✓
Educate patient and family on proper incision care, symptoms of SSI, and importance of reporting symptoms.	C	✓	✓	✓	✓

\*Grades are described in table 1. A represents the highest level evidence and I (insufficient) the lowest.

†Procedures are classified in table 3.

CSF, cerebrospinal fluid; SSI, surgical site infection; USPSTF, US Preventive Services Task Force.

- ▶ Biofilm (ie, aggregate of microorganisms) accumulation around implantable devices results in resistance to antimicrobial and antibiotic penetration. Level of certainty: high.
- ▶ Subfascial (deep) SSI associated with implantable pain devices typically requires system explant. Level of certainty: moderate.

#### Recommendations

- ▶ CBC with differential, ESR, and CRP measurements should be obtained and monitored for trends over time in patients presenting with suspected SSI. CRP is a more reliable biomarker for acute SSI than ESR, as ESR can remain elevated for a prolonged period after surgery. Blood cultures should be considered in the case of systemic signs of illness. Evidence: grade A.
- ▶ In the case of SSI requiring surgical debridement, irrigation, revision, or explantation, intraoperative cultures should be obtained, ideally including tissue, to guide selection of antibiotic therapy. Evidence: grade A.
- ▶ Complicated SSI involving neuraxial structures should be investigated with advanced imaging (eg, MRI when MRI conditionality is appropriate). A CSF evaluation should be conducted if meningeal signs are present. Evidence: grade A.
- ▶ Complete system explantation should be considered in cases of device-related SSI, particularly for deep (subfascial) and/or complicated device-related SSI. Evidence: grade A.
- ▶ High-volume, low-pressure irrigation with normal saline following debridement of necrotic tissue is recommended. Evidence: grade B.
- ▶ Antibiotic therapy should be guided by preoperative or intraoperative culture results when possible. Evidence: grade A.
- ▶ A trial of oral antibiotics may be considered in cases of superficial SSI with close clinical monitoring. This is typically offered for 7–10 days and should include an agent with

activity against staphylococcal and streptococcal species. Evidence: grade C.

- ▶ An antibiotic therapy plan should be developed with the help of an infectious disease specialist in cases of complicated SSI (including any involvement of neuraxial structures), systemic infection, multidrug-resistant infection, or for patients with pertinent medication allergies, chronic kidney disease, and/or with comorbidities placing them at elevated risk for resistant infection. Evidence: grade B.
- ▶ Consider consultation with an infectious disease specialist if reimplantation is planned following any deep and/or complicated device-related SSI. Evidence: grade A.
- ▶ A minimum 12-week interval is recommended prior to reimplantation in appropriate candidates following explantation for a device-related infection. Reimplantation at a site not involved in SSI should be considered. Evidence: grade C.
- ▶ Educate patient and family on proper incision care, symptoms of SSI, and importance of reporting symptoms. Evidence: grade C.

Table 11 summarizes all of the postprocedural recommendations.

#### **GUIDELINE CONSIDERATIONS, LITERATURE GAPS, AND FUTURE DIRECTIONS**

Creating a guideline that encompasses related yet disparate disciplines—such as regional anesthesia and pain medicine—is an ambitious task. There is a growing body of literature surrounding incidence of risk factors for and surgical techniques to reduce the incidence of SSIs of neuromodulation devices (SCS and IDDS) and regional anesthesia procedures. However, much can still be extrapolated from spine surgery literature, orthopedic literature, and even cardiac device literature about how to improve management of SCS and IDD devices, and many best practices originating from these other disciplines can be applied to

regional anesthesia and pain medicine. Likewise, best practices for incision closure and management do not need to be exclusive to the neuromodulation population to be informative. Additionally, catheter-based analgesia has reasonably solid literature for short-term application, but long-term utilization requires expert opinion and information from other disciplines such as peripherally inserted central catheterization procedures. While these limitations exist, they can also be viewed as strengths, as there is substantial evidence available to support a consensus.

Our recommendations, categorized as preprocedural (table 8), intraoperative (table 10), and postprocedural (table 11), represent the best currently available evidence, and can be implemented for pain procedures even as new research is occurring. The study of SSI risk mitigation is challenging and difficult. Many areas need more high-quality evidence and it is imperative that the current body of literature be reviewed frequently to help improve patient care and outcomes with the evidence that is available. Other surgical subspecialties have seen decreases in SSIs after the implementation of strategies developed from best practice infection control guidelines, such as spine surgery.<sup>680</sup> Specifically for implantable pain therapies, the introduction of an infection control bundle for SCS led to a 10-fold reduction in infection rate in a case series.<sup>681</sup> The intention of the infection control guidelines discussed here is to maintain this positive trend by increasing adherence to infection control measures and minimizing related complications. However, challenges like lack of staff training and time restrictions can hinder the application of these recommended practices. These guidelines aim to provide a framework for building educational tools for institutional training.

## CONCLUSIONS

In summary, these recommendations are intended to be a multidisciplinary functional set of guidelines to serve as a blueprint to guide clinical care and clinical decision-making in the regional anesthesia and chronic interventional pain practice. The issues addressed are constantly evolving, therefore, the creation of living documents that must be updated consistently will be required. These guidelines are not meant to suggest an unaltered standard of care that must be rigidly followed, rather they serve as the starting point for clinical decision-making, keeping in mind the unique patient characteristics in each case. Clinicians should always weigh the risks and benefits of each scenario to create personalized medicine. This guide represents the evidence-based approach to mitigation of risk of SSI in regional anesthesia and chronic interventional pain medicine.

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