

A Review of Surgical Techniques in Spinal Cord Stimulator Implantation to Decrease the Post-Operative Infection Rate

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Abstract

The use of spinal cord stimulator has been supported by the evidence-based studies at moderate level to control varying etiologies of pain. Infections are the most serious complications encountered in spinal cord stimulator implantation. The intent of this article is to present available studies and literature for surgical techniques to reduce the risks of postoperative wound infection for spinal cord implantation.

Keywords: Spinal cord stimulator; Neuromodulation; Surgical site infections; Wound infections; Surgical techniques; Antibiotic prophylaxis; Antibiotic irrigation

Review

The use of Spinal Cord Stimulator (SCS) to control various etiologies of pain has been supported by evidence-based studies at a moderate level. SCS has a positive, symptomatic, long-term effect in cases of refractory angina pain, severe ischemic limb pain secondary to peripheral vascular disease, peripheral neuropathic pain, chronic low-back pain, and in general is a safe and effective treatment for a variety of chronic neuropathic conditions [1]. It has been proven to help neuropathic pain [2], failed back surgery syndrome [3,4], and reflex sympathetic dystrophy [5-7]. SCS has also been used successfully for other pain issues such as critical lower limb ischemia [8], angina pectoris [9], central poststroke pain [10], renal pain [11], intractable visceral pelvic pain [12], and chronic visceral abdominal pain [13].

However, because of foreign body implantation, there has been a relatively high rate of reported complications from SCS implantation [14]. Bleeding/hematoma [15,16] and infections [17,18] are the most serious complications encountered in SCS implantations. Mekhail et al. [19] reviewed electronic medical records of 707 consecutive cases of patients who received SCS therapy and found that biologically related complications included pain at the generator site (12%) and clinical infection (4.5%; 2.5% with positive culture) which is higher than the infection rate for a clean wound. Deep wound infection from SCS implantation surgery often requires the removal of hardware followed by antibiotic administration. Rauchwerger et al. [18] revealed in his study that while a variety of bacteria may cause epidural abscess with spinal cord stimulation implantation, methicillin sensitive *Staphylococcus aureus*, and increasingly, Methicillin resistant *Staphylococcus aureus* (MRSA) and community-associated MRSA, are the most likely etiologic organisms. The reason for the high rate of infection is that many strains of coagulase negative staphylococci have the propensity to produce biofilm, allowing for adherence to medical devices. Spincemille et al. [20] reported technical problems and complications in a study of 60 patients with SCS implantation for critical limb ischemia. Technical problems such as loss of stimulation due to lead migration occurred in 13 patients (22%). Local infection at the site of implantation occurred in 3 patients (5%), resulting in a total complication rate of 27%. Premature depletion of the battery occurred within 2 years in 3 patients (5%). Ubbink et al. [21] analyzed six studies and reported complications of SCS treatment consisting of implantation problems (relative risk 9%) and changes in stimulation

requiring re-intervention (relative risk 15%). Infections of either the lead or the pulse generator pocket occurred less frequently (relative risk 3%).

Lead migration is the most common but potentially correctable problem in SCS implantation [22]. Rosenow et al. [23] analyzed a total of 577 procedures performed with percutaneous SCS and paddle leads, and found that 43.5% of SCS implantation involved revision or removal of SCS hardware. Approximately 80% of all leads were the percutaneous type. The majority (62%) of leads were placed in the thoracic region, and 33.5% of all leads required revision. Poor pain relief coverage was the most common indication for revision. They also found that surgically implanted leads broke twice as often as percutaneous leads. In 46% of the patients, hardware revision was required, and multiple revisions were necessary in 22.5% of cases. Laminectomy leads tended to break and migrate sooner than percutaneous leads. Thoracic leads became infected sooner than cervical leads.

Other rare complications of SCS implantation include spinal cord injury from direct needle insertion [24], myelopathy due to dense epidural scar tissue [25], and cerebral spinal fluid leak [26]. Meyer et al. [24] reported that a patient presented with upper and lower extremity weakness following inadvertent placement of an electrode into the spinal cord. Her neurologic status deteriorated in spite of successful removal of the electrode. Dam-Hieu et al. [25] reported on 2 cases of delayed compression of the cervical spinal cord by dense scar tissue forming around epidural electrodes implanted for SCS in 2010.

Despite the high risk of complications associated with spinal cord implantation, the success rate of SCS has been gradually improving with the development of technology and improvements in surgical technique. Pettit [27] reported in his article that the complications of sacral neuromodulation have been minimized as technology has improved. The main surgical complication remains surgical site infection. He reviewed evidence-based suggestions and procedure-

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specific techniques that reduced the infection rate to less than 2% in sacral nerve stimulation. A variety of surgical techniques have been employed to implant these devices such as one incision technique vs. two incisions technique. Infection rates associated with SCS vary depending on the surgical techniques used. With proper surgical technique, surgical skills may diminish the risk of infection with SCS implantation, potentiating the utility of this intervention.

Although improvements in medical technology and advances in operating room (OR) infection control practices have decreased postoperative wound infection rates significantly, aseptic technique has not completely eliminated bacterial contamination of the surgical field. The incidence of postoperative spinal infections varies from 0.4% to 3.5% depending on the type of wound conditions and the patient's comorbidity [28-30]. Surgical site infections (SSIs) are defined as infections occurring up to 30 days after surgery or up to one year after surgery in patients receiving implants [30]. The impact of surgical site infections in the United States has been estimated to cause billions in excess costs [31,32].

Despite the use of standard aseptic techniques, staphylococcal bacteria can still be isolated from the operative field regularly [33-35]. Postoperative wound infections are thought to commonly result from four possible mechanisms:

1. Direct contact contamination of the wound from OR personnel or instruments during surgery.
2. Airborne bacteria inoculation from the operating room environment [36,37]. Bacterial contamination from the air is influenced by the number of personnel and intensity of traffic within the OR at the time of surgery [36,38,39].
3. Colonization from a surgical site such as a small razor wound or a skin abrasion.
4. Hematogenous spreading of endogenous flora from a distant bacterial colonization or infection at a separate body site [40,41].

Procedure time and postoperative infection risk are positively correlated; i.e. the longer the procedure takes, the higher the risk for postoperative infections [42-44]. The rate of contamination of sterile instrument trays correlates with the duration such trays have been left exposed and uncovered. This further implicates air-borne bacteria as playing a significant role in SSIs [42,45]. Watanabe et al. [46] indicated that the incidence of infection positively correlated with longer operations [longer than 3 hours], delay to surgery following trauma, diabetes, and blood loss greater than 300 cc. There was no correlation with older age, BMI, or length of hospital stay prior to surgery.

SSIs have been closely correlated with intraoperative skin preparation. Maintaining aseptic technique may play an important role in decreasing postoperative wound infection. Chiang et al. [47] studied the data from 377 craniotomies/craniectomies with bone and flaps. They determined that operative factors such as the way the skin is prepared before incision rather than skin flora contaminants on the bone flaps may play an important role in the pathogenesis of SSIs after craniotomy/craniectomy.

The pathogens associated with postoperative wound infection in SCS implantation are similar to those in orthopedic or spinal surgery. Owens and Stoessel [31] suggested that the causative pathogens for postoperative wound infections depend on the type of surgery; the most commonly isolated organisms are *Staphylococcus aureus*, coagulase-negative staphylococci, *Enterococcus* spp. and *Escherichia coli*.

The Centers for Disease Control and Prevention guidelines for the prevention of SSIs emphasize the importance of good patient preparation, aseptic practice, and attention to surgical technique; antimicrobial prophylaxis is also indicated in specific circumstances [31].

Numerous patient-related and procedure-related factors influence the risk of SSI, and hence prevention requires a 'bundle' approach, with systematic attention to multiple risk factors, in order to reduce the risk of bacterial contamination and improve the patient's defenses.

Minimizing Risk factors and optimizing the patient's medical status before surgery

There are many factors affecting the wound healing process. Some of the risk factors may be not modifiable but some can be modified to decrease the risks for wound infection. However, some modifiable risk factor may not help to decrease wound infections if the duration of the modification is not long enough, such as obesity, smoking, etc.

Control of Diabetes mellitus: There are numerous studies showing that patients with uncontrolled diabetes mellitus have increased infection rates after major surgery [48-51]. Mehta [52] suggested that in the diabetic patient, intraoperative and perioperative modification of surgical technique, tight glycemic control, and other modifications can potentially yield improved clinical results for wound healing. Patients with uncontrolled diabetes mellitus should be evaluated and blood glucose levels should be optimized before the SCS implantation is planned.

Multidiscipline Modification for Malnutrition: Malnutrition can also increase surgical site infection. Gibbs et al. [53] in their study showed that a decrease in serum albumin from concentrations greater than 46 g/L to less than 21 g/L was associated with an exponential increase in mortality rates from less than 1% to 29% and in morbidity rates from 10% to 65% for surgery.

Obesity: Obesity may also increase SSIs [54-56]. Bamgbade et al. [57] analyzed adult postoperative complications from an electronic database covering 7,271 cases of postoperative complications that occurred within 30 days of noncardiac moderate or major surgery and revealed that obese patients had a higher prevalence of myocardial infarction [P = 0.001], peripheral nerve injury [P = 0.039], wound infection [P = 0.001], and urinary tract infection [P = 0.004].

Radiation therapy and Immunosuppression: History of irradiation at the site of the procedure may affect wound healing [58]. Use of immunosuppressants may cause an increase in SSIs [59]. Fortun et al. [60] studied a total of 1398 renal transplant recipients and found that the use of Sirolimus as maintenance therapy in kidney recipients is associated with a low rate of CMV infection and with a higher risk of surgical site infection.

Tobacco use: Tobacco use may lead to SSI, due to nicotine's effects of vasoconstriction and inhibition of wound healing [61,62]. Myles et al. [63] studied 489 adult patients undergoing ambulatory surgery and found that smoking was associated with an increased risk of respiratory complications and postoperative wound infection in ambulatory surgery patients. These findings warrant increased efforts at promoting smoking avoidance and cessation. Thomsen et al. [64] studied the data from a randomized controlled multicenter trial and found brief smoking intervention administered shortly before breast cancer surgery modestly increased self-reported perioperative smoking cessation without having any clinical impact on postoperative complications. However, Møller et al. [62] did a randomized trial in three hospitals in Denmark and found that an effective smoking intervention program

6-8 weeks before surgery reduces postoperative morbidity.

Alcohol Exposure: Nath et al. [65] studied the data from 7,631 patients with documented alcohol use (active alcohol use of at least two drinks per day within 2 weeks of surgery) that underwent elective surgery and found active alcohol consumption is a significant determinant of adverse outcomes in elective surgery. Patients with ETOH use who are scheduled to undergo elective surgery should be appropriately educated and counseled. Other studies [66] showed that heavy alcohol consumption increased the risk of nosocomial infection in men who underwent general surgical procedures.

Remote colonization of bacteria: Infection at sites remote from the operative field is also a host risk factor for postoperative infection that is potentially correctable prior to surgery [67]. Gupta et al. [68] analyzed postoperative MRSA clinical cultures and infections, total surgical site infections (SSIs), and surgical prophylaxis data among 4,238 eligible patients and found that preoperative nasal MRSA remained significantly associated with postoperative MRSA cultures and infections. The current recommendation is to aggressively treat remote infection prior to surgery.

Perioperative blood transfusion: Perioperative blood transfusion has been associated with an increased rate of postoperative infections, including wound infection, with donated white blood cell (WBC)-induced immunosuppression implicated as the culprit [69].

Steroid use: Ismael et al. [70] studied data of 635,265 patients and found that superficial surgical site infections (SSI) increased from 2.9% to 5% among 20,434 patients using steroids preoperatively (3.2%) (odds ratio, 1.724). Deep SSIs increased from 0.8% to 1.8% (odds ratio, 2.353). Organ/space SSIs and dehiscence increased 2 to 3-fold with steroid use (odds ratios, 2.469 and 3.338, respectively). Mortality increased almost 4-fold (1.6% to 6.0%; odds ratio, 3.920).

Hair removal: Hair removal with razor has been proven to increase SSIs [71]. For preoperative hair removal, methods that do not create microabrasions, such as clippers or depilatories, are preferred [72]. Alexander et al. [73] reported in a large randomized trial that SSIs decreased significantly following hair removal with clippers the morning of surgery compared with those who underwent day-of-surgery shaving with a razor. Some recommendations still advocate no preoperative hair removal [74].

Preoperative bathing with chlorhexidine: Preoperative bathing with chlorhexidine was commonly employed for a time; however some recent studies do not support it as an effective means to decrease SSIs. Webster [75] analyzed data from six trials with a total of 10,000 patients and concluded that the evidence does not support preoperative bathing with chlorhexidine as a means of reducing surgical site wound infection [76]. Chlorhexidine and alcohol is better than povidone-iodine antiseptics for surgery. Lee et al. [77] studied nine randomized controlled trials with a total of 3,614 patients included in the meta-analysis and found preoperative skin antiseptics with chlorhexidine is more effective than preoperative skin antiseptics with iodine for preventing SSI and results in cost savings [78,79]. Antiseptics with chlorhexidine and alcohol is recommended for spinal surgery by some neurosurgeons [80].

Epstein [80] recommended in his article additional preoperative, intraoperative, and postoperative methods of prophylaxis to further reduce spinal infection rates; 1. Nasal cultures and Bactroban ointment [mupirocin], and 2. Multiple prophylactic preoperative applications of chlorhexidine gluconate (CHG) 4% to the skin. Intraoperative prophylactic measures should not only include the routine use of an

antibiotic administered within 60 min of the incision, but should also include copious intraoperative irrigation (Normal Saline (NS) and/or NS with an antibiotic). Intraoperatively, instrumentation coated with antibiotics, and/or the topical application of antibiotics may further reduce the infection risk. Whether postoperative infections are reduced with the continued use of antibiotic prophylaxis remains controversial.

Antibiotic prophylaxis

Indication: In 2006, the Surgical Care Improvement Project (SCIP) developed out of the Surgical Infection Prevention (SIP) project and is continually evolving the manual guidelines to provide standard quality measures to unify documentation and track standards of care. Seven of the SCIP initiatives apply to the perioperative period: Prophylactic antibiotics should be received within 1 hour prior to surgical incision, be selected for activity against the most probable antimicrobial contaminants, and be discontinued within 24 hours after the surgery end-time [81].

Multiple studies have shown that a single preoperative dose of antibiotic is as effective as a full 5-day course of therapy. Prophylactic antibiotics should be administered within 1 hour prior to incision. Complicated, contaminated, or dirty procedures should receive additional postoperative coverage. The CDC recommends that antibiotic prophylaxis be used for all clean-contaminated procedures and certain clean procedures (i.e., those in which intravascular prosthetic material or a prosthetic joint will be inserted and those in which an incisional or organ/space SSI would pose catastrophic risk) [74]. Bratzler et al. [82] reviewed published guidelines for antimicrobial prophylaxis and concluded that infusion of the first antimicrobial dose should begin within 60 minutes before surgical incision and that prophylactic antimicrobial agents should be discontinued within 24 hours of the end of surgery [83]. Vancomycin should be started within 2 hours before incision due to extended infusion time. Other prophylactic antibiotics should be administered within 1 hour before skin incision. Thus far, the medical literature (with one cardiac surgery related exception) does not support the use of antibiotics beyond 24 hour post operatively, as this has failed to show any additional benefit.

Medications: The key in selecting an appropriate prophylactic antibiotic regimen with coverage against the expected endogenous flora at the surgical site depend on the type of surgery, as well as the anticipated organisms. The common bacteria encountered for wound infections after SCS implant are similar to those encountered in orthopedic surgeries. 1. *Staphylococcus aureus*, 2. coagulase-negative staphylococci; 3. streptococci 4. gram-negative rods/bacilli [74]. Based on the antibacterial spectrum and low incidence of allergy and side effects, the cephalosporins have traditionally been the drugs of choice for the vast majority of operative procedures especially for SCS implant [84]. Currently, cefazolin and cefuroxime are the preferred antibiotics for patients undergoing orthopaedic procedures. Clindamycin and vancomycin may be used for patients with a confirmed beta-lactam allergy. Vancomycin may be used in patients with known colonization with methicillin-resistant *S. aureus* (MRSA) or in facilities with recent methicillin-resistant *S. aureus* outbreaks. However, it should not be presumed that cephalosporins are the prophylactic agents of choice due to increase of antibiotic resistance. Antibiotics should always be carefully chosen for the targeted bacteria in each patient.

Vancomycin use should be discouraged for routine prophylaxis unless the patient is allergic to β -lactam antibiotics or the procedure involves implantation of prosthetic materials or devices at institutions with a high rate of infections caused by methicillin-resistant *Staphylococcus aureus* or methicillin-resistant coagulase

negative staphylococci. In particular, the emergence of Community-Associated-MRSA as a cause of SSI has clouded the issue of appropriate antimicrobial prophylaxis [85].

Chang et al. [86] suggested in their article that practical limitations that may affect the use of vancomycin in surgery include its narrow spectrum of antimicrobial activity and the need for a slow rate of infusion. Furthermore, the growing prevalence of vancomycin-resistant enterococci and the emergence of vancomycin-resistant *S. aureus* (VRSA) raise concerns about potential adverse effects on the antimicrobial susceptibility of nosocomial pathogens induced by the selective pressure of surgical antibiotic prophylaxis.

Timing of antibiotic administration: Suboptimal tissue levels and potentially increased risk of postoperative wound infection may result from antibiotic administration too early prior to the incision or after the time of incision. Surgical infections have been reduced by the administration of preoperative antibiotics within 60 minutes of surgery (incision) [56].

Some investigators found that SSI risk was lowest in those patients who received prophylaxis within 30 minutes (if given cephalosporins) or within 1 hour (if given vancomycin or a fluoroquinolone) prior to incision. Post-incision administration was associated with a significantly increased risk for SSI [87]. The Surgical Care Improvement Project (SCIP) over a 2-year period retrospectively looked at 6 variables to reduce postoperative complications, including surgical site infection due to the timely administration of preoperative antibiotics [88].

Administration of antibiotic immediately before incision may not provide enough time for tissue concentrations of the drug to reach the desired level at the time of incision. Weber and colleagues noted a twofold increase in the odds of SSI when cefuroxime prophylaxis was delivered less than 30 minutes before incision, as opposed to between 30 and 59 minutes pre-incision [89]. These results have also been reproduced in a study of 1,922 patients undergoing total hip arthroplasty in which the rate of SSI was lowest in those who received antibiotics 1 to 30 minutes before incision [90].

The SCIP quality improvement project defines appropriately timed antibiotic prophylaxis as delivery of the antibiotic within 1 hour prior to incision. The exceptions are that vancomycin and the fluoroquinolones should be given within 2 hours prior to incision because of the need for a longer infusion time. This definition has become widely used as a metric that indicates delivery of standard, high-quality surgical care [91].

A study of vancomycin use in cardiac surgery patients found that prophylaxis was most effective when given between 16 and 60 minutes before incision (relative risk (RR) = 7.8 compared to receipt between 15 and 0 minutes pre-incision) [92]. This may be explained by the need for an hour-long infusion of vancomycin to prevent infusion-related side effects, suggesting that only a small proportion of the dose had been infused at the time of the incision.

Dose of antibiotics: Forse et al. [93] suggested that the use of higher doses of antibiotic is probably needed for obese patients. Following administration of a 1 g dose of cefazolin, tissue and serum concentrations of the antibiotic were significantly decreased in morbidly obese patients when compared to non-obese controls.

However, another study of obese patients given 2 g doses of cefazolin found therapeutic tissue levels of the drug in only 48% of persons with a body mass index (BMI) between 40 and 49% in those with a BMI between 50 and 59, and 10% in those with a BMI 60 or higher, leading the authors to propose using continuous cefazolin administration in the morbidly obese patient to improve tissue concentrations [94].

Duration of antibiotics prophylaxis: A single dose of prophylaxis is necessary. At most, duration of antibiotic prophylaxis given should not be longer than 24 hr. Kanayama et al. [95] analyzed data from 1597 consecutive uninfected patients who had undergone lumbar spine surgery between January 1999 and September 2004 and concluded that based on the CDC guideline, a single dose of antimicrobial prophylaxis was proven to be efficacious for the prevention of SSI in lumbar spine surgeries. A shorter duration of first-generation cephalosporin use may effectively prevent the emergence of antibiotic-resistant bacterial infection. Harbarth et al. [96] found that prolonged antibiotic prophylaxis (>48 hours post-incision) has been significantly associated with an increased risk of acquiring an antibiotic-resistant pathogen.

Additional IV antibiotics may be necessary in prolonged surgery lasting over three hours. Dellinger et al. [97] found that as critical as it is to provide an appropriately timed initial dose of antibiotic, it is also essential to ensure that tissue concentrations remain well above the minimum inhibitory concentration (MIC) values of common pathogens during the entire procedure. To achieve this goal, antibiotics should also be re-administered during long surgical procedures.

Use of Epinephrine with local anesthetic

Epinephrine has long been employed in surgery as a potentiator of local anesthetic. The vasoconstrictive properties of epinephrine act to decrease the systemic absorption of local anesthetic and thereby increase the duration of anesthetic effect within target tissues. It has been approved for safe use in general surgery and non-implantation surgery for some time. It's most commonly used in procedures involving regions of rich blood flow such as the scalp and face. Another benefit to the use of epinephrine in local anesthetic is to achieve better hemostasis when substantial topical blood loss is anticipated, particularly in case of large wounds [98].

Many studies have been done to evaluate the influence of epinephrine on the incisional healing processes. Some studies have shown that the presence of epinephrine in lidocaine solution had no significant role in the delay of the wound healing process [99]. Wakamatsu [100] suggested that a local anesthetic without a vasoconstrictor does not modify the postextraction wound healing process. He argued that epinephrine does not prolong and will actually promote wound healing based on his study of wound healing following tooth extraction. However, the study was done in the facial region which has a very rich blood supply. The study did not address wound healing at the primary surgical incision site of a region that is less well vascularized. Surgery at a region of poor blood supply may show a different response to the use of epinephrine.

The next question regarding the use of epinephrine with a local anesthetic involves its affect on the postoperative infection rate. Parr et al [101], in his in vitro study, found that skin anesthetized with Lidocaine demonstrated a dose-dependent growth inhibition for some strains of bacteria such as *Enterococcus faecalis*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*. He also suggested that the addition of epinephrine to the local anesthetic had no effect on the susceptibility of the bacteria to lidocaine. However, this in-vitro study does not address the question of rich vs poor blood supply when evaluating the impact of epinephrine on postoperative wound infection.

To date, there are no large scale randomized control studies regarding the impact of epinephrine use on postoperative infection rate. Stratford et al. [102] demonstrated that lidocaine use prior to inoculation of bacteria was associated with a greater than 70% decrease

in bacterial count in their *in vivo* study (lidocaine infiltration vs. pre-infiltration of lidocaine in a guinea pig model). Conversely, the addition of epinephrine (1:100,000) to lidocaine was associated with a 20-fold increase in bacterial count compared with control values (lidocaine with epinephrine infiltration vs pre-infiltration of lidocaine). This is the first study using an *in vivo* surgical wound model to demonstrate inhibition of bacterial growth by a local anesthetic, and a subsequent reversal of this protective effect with the addition of epinephrine. Moreover, when epinephrine is used, there is a substantial increase in bacterial growth, suggesting epinephrine may increase risk of surgical wound infection

Systemic increase of epinephrine from surgery related stress may cause impairment of wound healing. Sivamani et al. [103] suggested that burn wounds generate epinephrine locally in response to injury. Epinephrine levels are locally, as well as systemically elevated, and wound healing is impacted by these dual mechanisms. Treatment with beta adrenergic antagonists significantly improves the rate of burn wound re-epithelialization. This work suggests that specific beta2AR antagonists may be apt, near-term translational therapeutic targets for enhancing burn wound healing. Romana-Soza et al. [104] published an article in 2009 which suggested that high epinephrine concentrations related to stress, increased murine skin fibroblast proliferation and nitric oxide synthesis, and strongly inhibited skin fibroblast migration.

No study to date has been done to determine the exact mechanism as to how epinephrine acts to increase wound infection rate. Rodrigues et al. [105] suggested that Lidocaine blocks nociceptive fibers, preventing initial wound signaling and mast cell degranulation. It is hypothesized that epinephrine and buffer affect wound healing by potentiating lidocaine blockage. Epinephrine may be used in non-implantation SCS trials as bacteria in these circumstances are accessible to humoral immunity. Conversely, the advent of bacterial seeding of hardware remains a challenging issue in SCS implantation since antibiotic therapy cannot be delivered to an area inaccessible to body fluid.

In order to minimize tissue damage and decrease postoperative infection rate, epinephrine should be used with extreme caution.

Antibiotic irrigation

Intraoperative antibiotic wound lavage has been used for many decades. Lord et al. [106] analyzed data for vascular surgeries and revealed that in clean operations without antibiotic wound lavage there was a 0.73% rate of in-hospital wound infections in 685 patients. In contrast, there was zero rate of infection in 760 patients who underwent intraoperative wound lavage throughout the operative procedure.

There are some studies indicating saline irrigation helps to decreased bacteria within surgical wounds [46,107,108].

Whether antibiotic irrigation helps to decrease wound infection rate in clean or clean-contaminated surgeries is debatable. In most cases, bacterial seeding of deep wounds occurs through air droplet or direct contact. Theoretically, antibiotic irrigation should further decrease wound infections. However, some studies showed no benefits from antibiotic irrigation to decrease infection rate during surgery. Savitz et al. [109] stated in his study that although the virtual elimination of bacterial growth in the surgical site was accomplished, the efficacy of topical antibiotics in the prevention of wound infection remains unproven.

Others studies have advocated the benefit of antibiotic irrigation to decrease wound infection rate.

Gallup [110] determined in a 1996 study that the use of antibiotic

prophylaxis of wounds in a select patient population resulted in fewer wound complications. Similarly, Pfeiffer et al. [111] reported their clinical data to support the use of topical antibiotics and antibiotic irrigation in cosmetic breast surgery. He reported significant increases of both infections and seroma in patients not treated with topical antibiotics and antibiotic irrigation, compared with a cohort of similar patients where topical antibiotics were used. Bergamini et al. [112] suggested in his study that when wound contamination is great, a combination of topical and systemic antibiotics is the more effective regimen. Where wound contamination is less severe, systemic antibiotic prophylaxis is all that is required; no further benefit is obtained by the additional administration of topical antibiotics. Dirschl et al. [113] published his article indicating that:

1]. Although the orthopedic literature on the clinical use of topical antibiotics is sparse, the effectiveness of topical antibiotics has been shown well enough *in vitro* and in the surgical literature to justify strong consideration of their use in orthopedic procedures.

2]. Saline irrigation should not be relied upon to reduce bacterial contamination completely, although it does remove debris, foreign material, and clot, which often contain bacteria, from the surgical wound.

3]. Topical antibiotic agents used for irrigation should have a broad spectrum of antimicrobial activity. Triple antibiotic solution [neomycin, polymyxin, and bacitracin] provides the most complete coverage against the organisms most likely to cause infections in both clean and contaminated orthopedic surgical cases. These agents should be allowed to remain in the wound for at least 1 minute before their removal.

4]. Further studies of topical antibiotic irrigation in orthopedic surgery are needed to demonstrate the most effective antibiotic[s] and technique of administration.

Early and frequent wound irrigation has been demonstrated to lead to a lower rate of wound complications. Owens et al. [114] found that earlier irrigation in a contaminated wound model resulted in superior bacterial removal. Most recently in 2010, Sookpotarom et al. [107] found that vigorous antibiotic wound irrigation demonstrated a low rate of wound complications.

There is further indirect evidence to support antibiotic irrigation, such as antibiotic-impregnated cement and beads to decrease wound infection for orthopedic implant surgery, first introduced in 1939 [115]. Bourne [116] advocated that the use of antibiotic-impregnated cement [in conjunction with systemic prophylaxis] was associated with significant reduction in SSIs in studies from several large clinical registries in Europe [117].

Copious intraoperative irrigation (normal saline (NS) and/or NS with an antibiotic) to further reduce the infection risk in spinal surgery has been recommended by neurosurgeons [80]. Maurice-Williams et al. [118] did a study on a series of 1173 clean neurosurgical operations compared with a control of 303 operations. Both treatment and control groups were operated on by the same surgeon, using similar surgical techniques. The control group received parenteral pre- and postoperative antibiotics (flucloxacillin and ampicillin). The treatment group (where the parenteral antibiotics used was cephadrine) also received wound irrigation with a solution of gentamicin and flucloxacillin. The infection rate was 0.42% in the treatment group (five patients), in the control group it was 3.96% (12 patients). The difference was highly significant ($p = 0.00006$).

Spinal cord stimulator implantation surgery carries high risks for postoperative wound infection because the implanted pulse generator has an irregular surface. The niches on the irregular surface of the implanted pulse generator may potentially prevent body fluid to access and eradicate the inoculated bacteria. In some orthopedic procedures, in order to decrease bacteria seeding, the irregular surfaces on implanted hardware have prompted the use of antibiotic coating of these surfaces. An antibiotic irrigation should be used every 10-15 minutes to irrigate the wound with antibiotic saline solution. After the pocket is created, it should be also irrigated and packed with gauze soaked with antibiotic irrigation solution before it is closed.

A variety of antibiotics can be chosen for antibiotic irrigations, such as bacitracin, bacitracin with polymyxin, neomycin, cephalosporins, clindamycin, etc. The antibiotic chosen for irrigation should be carefully selected based on the targeted bacteria.

Caution must be applied to use antibiotics in irrigation. Some antibiotics can cause severe adverse effects and allergic reactions. Anaphylaxis has been reported in reaction to bacitracin irrigation during surgery [119]. Damm [120] reported that three patients developed severe adverse reactions after prophylactic bacitracin irrigation concentrated at 50,000 units per 10 mL. Two of these events occurred during pacemaker insertions and the other during a cardiac resynchronization defibrillator implantation.

Optimizing the patient's medical status during surgery to decrease possible wound infection

Evidence based studies show that normothermia, normoglycemia, oxygen delivery and use of appropriate antibiotics have significantly reduced SSIs.

Moucha et al. [121] emphasized in their article that multiple risk factors for surgical site infection have been identified. Some of these factors directly affect the wound-healing process, whereas others can lead to blood-borne sepsis or relative immunosuppression. Modifying a patient's medications, screening for comorbidity, such as HIV or diabetes mellitus, and advising the patient on options to diminish or eliminate adverse behaviors, such as smoking, should lower the risk for surgical site infections.

Optimizing the patient's oxygen: Dellinger et al. [122] suggested in his study that optimizing the patient's oxygen saturation during surgery may also decrease SSIs. Another study also showed that supplemental perioperative oxygen may reduce the incidence of surgical-wound infection [123].

Maintaining the patient's body temperature: Maintaining the patient's body temperature and avoiding hypothermia may decrease SSIs. Kurz et al. [124] did a randomized study on two hundred patients undergoing colorectal surgery and found that hypothermia itself may delay healing and predispose patients to wound infections. He suggested that in patients undergoing colorectal resection, maintaining normothermia intraoperatively was likely to decrease the incidence of infectious complication, as well as shorten hospitalizations.

Stress: Severe stress may also cause an increase in SSIs. The systemic response to injury is characterized by massive release of norepinephrine (NE) into the circulation as a result of global sympathetic activation. Multiple authors have demonstrated NE-mediated alterations in migration of circulating neutrophils to wounds [125]. Romana-Souza et al. [104] suggested in his study that high epinephrine concentrations increased murine skin fibroblast proliferation and nitric oxide synthesis, and strongly inhibited skin fibroblast migration.

Additionally, Lidocaine blocks nociceptive fibers, preventing initial wound signaling and mast cell degranulation.

Surgical skills for SCS implantation

In order to improve the success rate of SCS implantation, some special modifications in surgical technique may be employed. The main goal of the modifications is to minimize tissue damage and decrease or eradicate bacterial seeding of the surgical wounds.

Tissue damage should be minimized, as surgical wound size has been found to correlate with increased rate of SSIs: In clean and clean-contaminated surgical procedures, quantitative bacterial inoculation of the wound in areas of microscopically devitalized tissue provide a niche; a small bacterial inoculum may grow in relative isolation from the host's defenses, playing a major role in the pathogenesis of infection [126].

In order to decrease the rate of SSI in SCS implantation, the incisions should be made with a scalpel with a clear cut, and the tissue should be handled with care. Excessive blunt dissection should be avoided to achieve minimal tissue damage. The size of the surgical wound should be as small as possible without obscuring the view of the surgery. This is particularly important at the SCS battery site, as Kaafarani et al. [127] found that large surgical wound size correlated with an increased rate of SSI's, when he compared open ventral incisional hernia repair vs laparoscopic incisional hernia repair. The battery pocket should not be configured larger than the battery size. The goal when creating the battery pocket is to decrease dead space within the pocket, so that the battery will not flip at a later time. Minimizing dead space within the pocket also limits seroma development which can serve as a medium for bacterial growth.

Excessive use of Electrocauterization as means of coagulative necrosis may increase the rate of

SSIs: Soballe et al. [128] found that coagulative necrosis induced by cautery of blood vessels most likely limits the ability of antibiotics to reach the wound bed during the early postoperative period.

Yilmaz et al. [129] compared scalpel, electrocautery and ultrasonic dissector effects to impact on wound complication and demonstrated in terms of tissue destruction there is a higher incidence of pro-inflammatory media with electrocautery use. TNF- α and IL-6 levels were significantly higher in samples obtained from the drains of patients operated with electrocautery.

Parlakgumus et al. [130] found in a prospective randomized clinical trial that monopolar electrocautery has worse wound healing than a tissue sealing-cutting device. The main outcomes measured were surgical site infection, early wound failure (dehiscence), and unhealed wound rate.

Development of wound infection reflects an imbalance between the bacterial mediated tissue destruction and the eradication ability of the host immune system. The function of eradication is primarily mediated by neutrophil, macrophage cells with antibodies and complement, which facilitate the process of phagocytosis [131].

Excessive use of Electrocauterization, may also delay macrophage/neutrophils migration to the wound, due to isolation of tissue as a result of thermal coagulation. It may delay the removal of dead tissue and bacteria. Minimal use of electrocautery is encouraged, in order to avoid heavy thermal damage to the underlying tissues, which may inhibit wound healing; especially, since infection rate is correlated with the severity of tissue damage. Thus, during SCS implantation, bleeding

should be controlled by the application of direct pressure, and light use of Electrocauterization.

Prolonged surgical procedure time is correlated to SSIs: During the SCS implantation procedure, one must follow strict adherence to sterile technique to minimize risk of infection. Although absolute sterility of the surgical field cannot be achieved due to airborne bacteria, one may decrease the risk of airborne bacterial contamination of the surgical wound through decreased surgical time. Prolonged surgical procedure time [greater than 5 hours] will significantly increase the postsurgical infection rate. In a 2011 study exploring post-op wound infection, Bucher et al. [44] showed increased procedure duration of implantable devices as a positive correlate with development of a surgical site infection. The level of airborne bacteria should also be reduced by limiting the number of personnel in the OR, as well as limiting the traffic through the operating room at the time of the procedure.

All operating Room should be maintained at positive pressure with respect to the corridors and adjacent areas. The positive pressure should prevent airflow from less clean areas into more clean areas. All air should be introduced from the ceiling and exhausted at the floor. The positive air pressure and lamellar air flow inside the operating room may help to decrease SSIs.

Surgical techniques and instrumentation used in surgery may also directly affect SSIs: Investigational models have demonstrated how the technical variables of the surgical procedure influence the risk of infection. McGeehan suggested in his study that some suture materials appear to have a stronger adjuvant effect on infection than others, and that certain suture materials produce conditions unfavorable to multiplication of bacteria [132]. In addition, different suture types have a different impact on wound healing and affect the wound infection rate significantly [126].

Suture Types

For incision closure, simple interrupted sutures are recommended due to their greater tensile strength compared to running sutures. Also, with interrupted sutures, there is less potential for causing wound edema and impaired cutaneous circulation, which may predispose to impaired wound healing and infection. Also, it is recommended that the suture length-wound length ratio be controlled to around 4-5. Too many stitches may provide loci for bacterial anchoring, and thus increase the chance of infection. Conventional simple running suture in deep tissue is not recommended as it does not hold the wound together well under tension. Additionally, a wound infection from a conventional running suture may affect a larger wound area (Table 1).

Running locked sutures are highly discouraged during SCS implantation for wound closure, as they may impair the microcirculation surrounding the wound. Running locked sutures may cause tissue strangulation due to increased tensile strength if placed too tightly. This type of suture should be used only in areas with good vascularization and requiring additional hemostasis such as scalp, etc.

In summary, the suture technique that is most favorable for wound closure is the conventional interrupted suture. Simple running suture may be used for subcuticular closure. Stapling is not recommended. Smith et al. [133] studied data from 683 surgical wounds and found a significantly higher risk of developing a wound infection with staple closure when compared to suturing.

Size of Stitches

The incision closure should be performed in at least three layers

(deep, intermediate and superficial/subcuticular).

The sutures should be placed at least 5-8 mm from the wound edge and about 8-10 mm apart, holding approximately 8 mm of tissue depth. To avoid tissue strangulation, the sutures should not be tied too tightly. It is necessary to keep at least 5 mm of space between stitches horizontally and vertically. This will allow proper blood supply to tissues between stitches and decrease the risk of tissue strangulation, which may lead to improper healing, and infection. The key to closure is to approximate wound edges with minimal tissue tension.

Larger stitches (bigger bites) horizontally and vertically are not recommended. Millbourn et al. [134] did a clinical study, where 321 patients were randomized to closure with small stitches (stitches placed 5-8 mm from the wound edge and less than 5 mm apart) and 370 with large stitches (stitches, placed more than 1 cm from the wound edge). They found that infection and herniation were less common with small stitches. With small stitches, there were no identified risk factors for infection or herniation. With large stitches, wound contamination and the patient being diabetic were independent risk factors for infection, and long operation time and surgical site infection were risk factors for herniation.

Surgical knots: Reduced knot size is recommended to avoid excessive tissue reaction to both absorbable and non-absorbable sutures. Excessive tension with suture tying used for approximation should be avoided, as this may also contribute to tissue strangulation, delayed healing, and infection.

Wound Cover: The goal of using wound dressing is to keep the wound clean and dry, and to prevent favorable conditions for bacterial growth. Sterile strips applied vertically across the wound and spaced 1-2 mm apart between sterile strips allow for fluid drainage if subcuticular sutures are used. The reason to apply the sterile strips vertically across the wound is to hold the edges of wound together to prevent wound separation.

Sterile gauze and Tegaderm may be applied to the wound. Small needle holes should be created on the Tegaderm during summer time to keep moisture away from the wound. The dressing may be removed and the wound can be opened to air 24 hours after the surgery. The key is to keep the wound clean and dry. Removal of suture: interrupted nylon sutures should be removed in 7-10 days.

*Anchoring leads

This is the technique used by the author to anchor the spinal cord stimulator leads. It demonstrates one of the many techniques on how to anchor the leads with minimal suture and without strangulation of tissues.

The needles are removed with a push-pull technique under fluoroscopic monitoring with careful attention to avoid lead retraction. Two anchors are then bathed in antibiotic solution. The leads are then passed through the anchors until the anchors enter the needle tract. Double -eight anchoring technique is used to fix the anchor in place. The long axis of the anchor should be pointing in the direction of the epidural entry point. The double-eight technique is used to ensure proper anchor fixation with minimal use of silk suture.

The double figure eight technique (Figure 1)

First, use a 2-0 silk suture needle to grasp the deeper fascia and soft tissue at one side of both of the leads. This will firmly hold the deeper fascia tissue with a suture loop, but not strangulating the tissue (Figures 1A and 2). The suture loop should be loose enough to avoid

Sutures	Tensile strength	Absorption rate	Reaction	Common use	Knot typing
Vicryl (the term "vicryl" has been used generically referring to any synthetic absorbable suture made primarily of polyglycolic acid.)	Reduce to 65% 2 weeks	Absorbed by hydrolysis in 60-70 days	Mild	Soft tissue approximation and/or ligation, but not for use in cardiovascular or neurological tissues.	Square Knot Surgeon's or Friction Knot
Silk (Braided)	Progressive degradation of fiber may result in gradual loss of tensile strength over 1 year	Gradual encapsulation by fibrous connective tissue. Absorbed in 2 years	Moderate	Ligation	Square Knot (May cause Acute inflammatory reaction)
Monocryl (poliglecaprone 25)	tensile strength is at 50-60% undyed (60-70% dyed), at 2 weeks its 20-30% undyed (30-40% dyed),	91-119 days	Low	Rarely used for percutaneous skin closure, and is not used in areas of high tension. (may use for subcutaneous approximation)	Square Knot (less of a tendency to exit through the skin after it breaks down)
Nylon	Dec. 15% in 1 year	Non-absorbable	Low	skin closure (Monofilament)	Square Knot Surgeon's or Friction Knot Needs six or more loops to keep tension

Table 1: Possible Sutures used in this SCS implant.

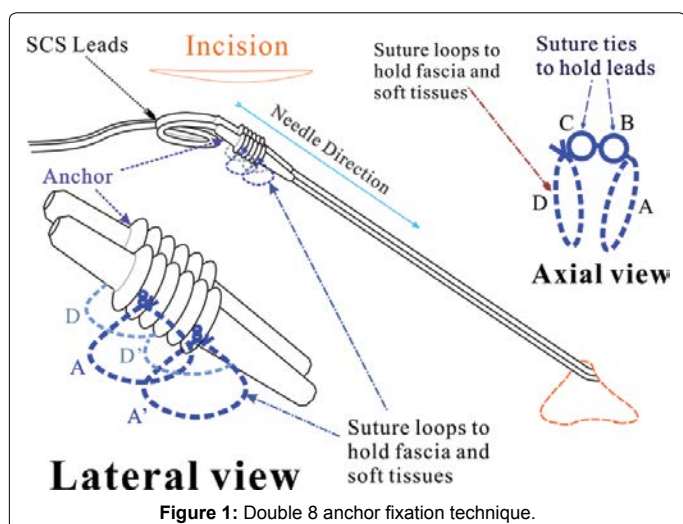


Figure 1: Double 8 anchor fixation technique.

tissue strangulation. A minimum of three throw knots are required to adequately hold the tissue.

Then you will tightly tie the closer lead (Figures 1B and 3). The suture knot should be gradually pulled with tension allowing for a tie of maximal tightness to firmly hold the lead anchor in place. A minimum of three throw knots are required to adequately hold the first anchor with the lead.

Then tightly tie the second lead with the same technique (Figures 1C and 4) as above.

Use the needle to vertically grasp the deeper fascia and soft tissue on the other side of the leads and tie the tissue firmly with three throw knots. Careful consideration again must be paid to avoid tissue strangulation when performing these ties (Figures 1D and 5).

The same technique is used to tie the anchor about 5 mm away from the first double-eight tie. You will suture the anchors in the same direction as the leads are introduced by the toughy needles (Figure 6).

Conclusion

The intent of this article is to review current studies on surgical site infection related to surgical techniques (Table 2), and to help pain physicians reduce the risks of postoperative wound infection

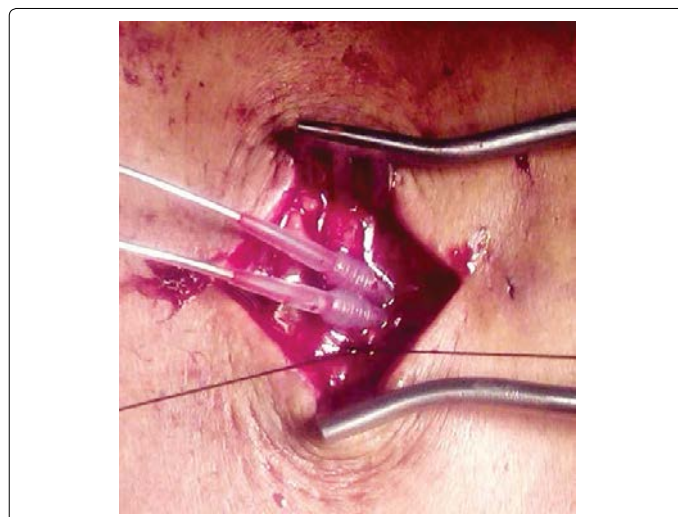


Figure 2: Use a 2-0 silk suture needle to vertically grasp the deeper fascia and soft tissue at one side of both leads and firmly hold the deeper facial tissue with a suture loop, but not strangulate the tissue. It is necessary to use three throw knots to separate the low tension (soft tissue) loop from the high (anchor/lead) tension loop.

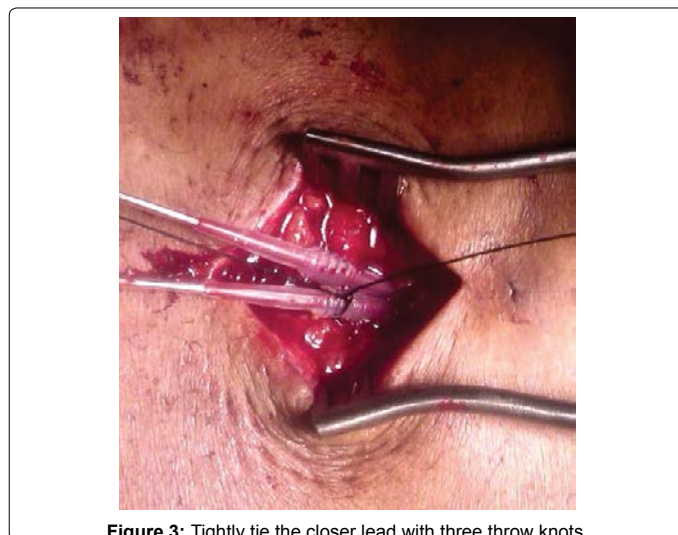


Figure 3: Tightly tie the closer lead with three throw knots.

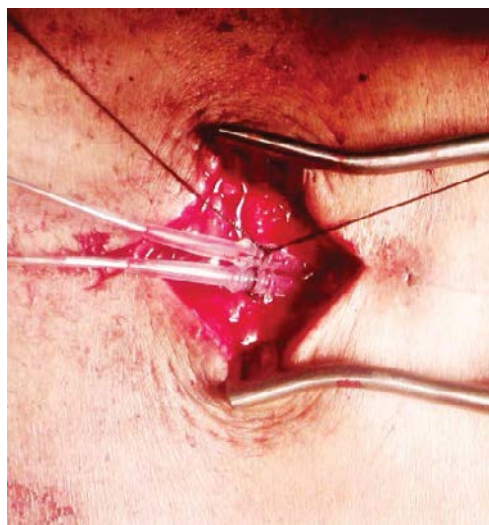


Figure 4: Then tightly tie the second lead with the same technique.

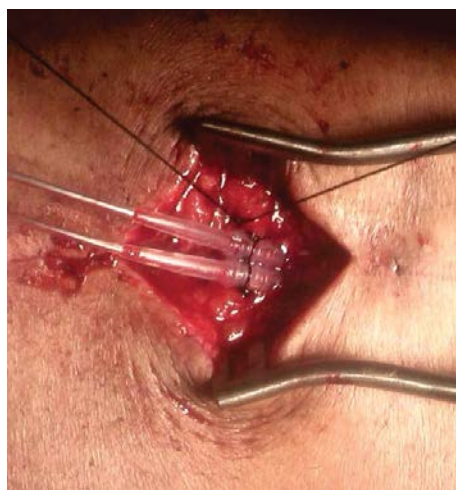


Figure 5: Use the needle to vertically grasp the deeper fascia and soft tissue on the other side of the leads/anchors and tie the fascia and soft tissue firmly with three throw knots without strangulating the tissue.

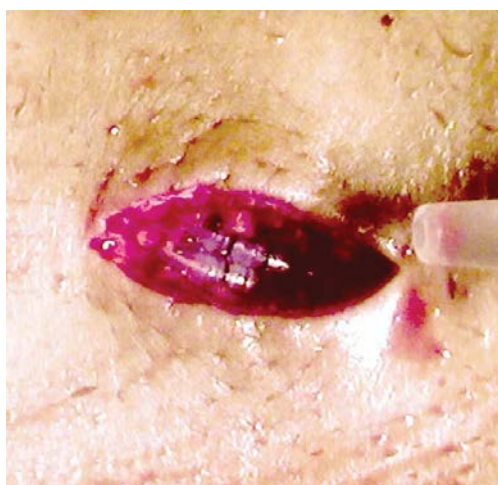


Figure 6: The same technique is used to tie the leads/anchors once again about 5 mm away from the first double 8 tie to fix the leads and anchors in the same direction as the leads introduced by the needles.

Timing	Goal	Surgical Techniques to Reduce SSIs	
Pre-operative	Minimize Risk Factors and Optimize the Patient's Medical Status	Control of diabetes mellitus	
		Correct malnutrition or obesity prior to surgery	
		Avoid surgery during radiation therapy and immunosuppression if possible	
		Eliminate alcohol abuse and smoking before planning surgery	
		Control all localized infection or bacteria colonization such as remote skin infection or UTI	
		Limit perioperative blood transfusions or systemic steroid usage	
		Preoperative bathing with soap or chlorhexidine if possible	
		No preoperative hair removal	
Intra-operative	Strictly Follow Aseptic Technique and Minimize Bacteria Exposure	Positive air pressure and laminar air flow inside the operating room as per the recommendations of the CDC and Healthcare Infection Control Practices Advisory Committee	
		Sterility of surgical field	
		Limit surgical time	
	Optimize the Patient's Conditions	Limit operating room personal in/out of the operating room	
		Optimize the patient's oxygen	
		Maintain the patient's body temperature	
		Minimize the patient's stress with sedatives	
		Minimize Tissue damage	Minimize or avoid the use of epinephrine
			Small clear cut incision with a scalpel
			No excessive use of electrocautery and minimize blunt dissection to achieve minimal tissue damage.
Intraoperative antibiotic wound lavage/irrigation			
Post-operative	Optimize Wound Healing and Decreasing Possible Wound Infection	Anchor the leads with an optimized technique*	
		Make sure the battery pocket is not configured larger than the battery size. Close all potential dead space within the small battery pocket with a good suture technique.	
		Wound closure with optimized surgical technique using the best size and type of suture.	
Post-operative	Optimize Wound Healing and Decreasing Possible Wound Infection	Keep wounds dry and clean. Instruct the patient to change the dressings as needed.	

Table 2: Optimized techniques to reduce SSIs.

in spinal cord implantation. To achieve this, physicians should limit tissue damage, and decrease bacterial inoculation of the surgical wound. Tissue damage should be limited through avoiding the use of epinephrine, controlling the length of the surgical incision and the amount of dissection needed for the battery pocket, gentle handling of soft tissues and avoiding tissue strangulation when suturing.

To decrease bacterial inoculations, antibiotic prophylaxis should be routinely used. The selection of antibiotic is based on the patient's conditions, as well as the targeted bacteria. The goal is to prevent blood transmission of bacteria from a remote body site, or of bacteria inoculated in the deep tissue of the wound during surgery. Antibiotic irrigation during the implantation surgery should be frequently used to wash out any airborne bacterial seeding. Furthermore, the operating room personnel, in terms of number and movement in and out of the operating room during the surgery should also be controlled to

minimize the contamination by airborne bacteria. The above efforts may allow the rate of surgical site infection and wound complications to be controlled to a minimal level, thus potentiating the utility of SCS in the chronic pain patient.

References

1. Cameron T (2004) Safety and efficacy of spinal cord stimulation for the treatment of chronic pain: a 20-year literature review. *J Neurosurg* 100: 254-267.
2. Simpson EL, Duenas A, Holmes MW, Papaioannou D, Chilcott J (2009) Spinal cord stimulation for chronic pain of neuropathic or ischaemic origin: systematic review and economic evaluation. *Health Technol Assess* 13: iii, ix-x, 1-154.
3. Manchikanti L, Boswell MV, Singh V, Benyamin RM, Fellows B, Abdi S, et al. (2009) Comprehensive evidence-based guidelines for interventional techniques in the management of chronic spinal pain *Pain Physician* 12: 699-802.
4. Hieu PD, Person H, Houidi K, Rodriguez V, Vallee B, et al. (1994) [Treatment of chronic lumbago and radicular pain by spinal cord stimulation. Long-term results]. *Rev Rhum Ed Fr* 61: 271-277.
5. Kemler MA, de Vet HC, Barendse GA, van den Wildenberg FA, van Kleef M (2008) Effect of spinal cord stimulation for chronic complex regional pain syndrome Type I: five-year final follow-up of patients in a randomized controlled trial. *J Neurosurg* 108: 292-298.
6. Kemler MA, Barendse GA, van Kleef M, de Vet HC, Rijks CP, et al. (2000) Spinal cord stimulation in patients with chronic reflex sympathetic dystrophy. *N Engl J Med* 343: 618-624.
7. Ahmed SU (2003) Complex regional pain syndrome type I after myocardial infarction treated with spinal cord stimulation. *Reg Anesth Pain Med* 28: 245-247.
8. Colini Baldeschi G, Carlizza A (2011) Spinal cord stimulation: predictive parameters of outcome in patients suffering from critical lower limb ischemia. A preliminary study. *Neuromodulation* 14: 530-532.
9. Andersen C (1997) Complications in spinal cord stimulation for treatment of angina pectoris. Differences in unipolar and multipolar percutaneous inserted electrodes. *Acta Cardiol* 52: 325-333.
10. Aly MM, Saitoh Y, Hosomi K, Oshino S, Kishima H, et al. (2010) Spinal cord stimulation for central poststroke pain. *Neurosurgery* 67: ons206-212.
11. Kim CH, Issa M (2011) Spinal cord stimulation for the treatment of chronic renal pain secondary to uretero-pelvic junction obstruction. *Pain Physician* 14: 55-59.
12. Kapural L, Narouze SN, Janicki TI, Mekhail N (2006) Spinal cord stimulation is an effective treatment for the chronic intractable visceral pelvic pain. *Pain Med* 7: 440-443.
13. Kapural L, Deer T, Yakovlev A, Bensitel T, Hayek S, et al. (2010) Technical aspects of spinal cord stimulation for managing chronic visceral abdominal pain: the results from the national survey. *Pain Med* 11: 685-691.
14. Pineda A (1978) Complications of dorsal column stimulation *J Neurosurg* 48: 64-68.
15. Franzini A, Ferroli P, Marras C, Broggi G (2005) Huge epidural hematoma after surgery for spinal cord stimulation. *Acta Neurochir (Wien)* 147: 565-567.
16. Chiravuri S, Wasserman R, Chawla A, Haider N (2008) Subdural hematoma following spinal cord stimulator implant. *Pain Physician* 11: 97-101.
17. Arxer A, Busquets C, Vilaplana J, Villalonga A (2003) Subacute epidural abscess after spinal cord stimulator implantation. *Eur J Anaesthesiol* 20: 755-757.
18. Rauchwerger JJ, Zoarski GH, Waghmarae R, Rabinowitz RP, Kent JL, et al. (2008) Epidural abscess due to spinal cord stimulator trial. *Pain Pract* 8: 324-328.
19. Mekhail NA, Mathews M, Nageeb F, Guirguis M, Mekhail MN, et al. (2011) Retrospective review of 707 cases of spinal cord stimulation: indications and complications. *Pain Pract* 11: 148-153.
20. Spincemaille GH, Klomp HM, Steyerberg EW, van Urk H, Habbema JD; ESES study group (2000) Technical data and complications of spinal cord stimulation: data from a randomized trial on critical limb ischemia. *Stereotact Funct Neurosurg* 74: 63-72.
21. Ubbink DT, Vermeulen H (2005) Spinal cord stimulation for non-reconstructable chronic critical leg ischaemia. *Cochrane Database Syst Rev* 20: CD004001.
22. Rainov NG, Heidecke V (2007) Hardware failures in spinal cord stimulation (SCS) for chronic benign pain of spinal origin. *Acta Neurochir Suppl* 97: 101-104.
23. Rosenow JM, Stanton-Hicks M, Rezaei AR, Henderson JM (2006) Failure modes of spinal cord stimulation hardware. *J Neurosurg Spine* 5: 183-190.
24. Meyer SC, Swartz K, Johnson JP (2007) Quadriparesis and spinal cord stimulation: case report. *Spine (Phila Pa 1976)* 32: E565-568.
25. Dam-Hieu P, Magro E, Seizeur R, Simon A, Quinio B (2010) Cervical cord compression due to delayed scarring around epidural electrodes used in spinal cord stimulation. *J Neurosurg Spine* 12: 409-412.
26. Eldrige JS, Weingarten TN, Rho RH (2006) Management of cerebral spinal fluid leak complicating spinal cord stimulator implantation. *Pain Pract* 6: 285-288.
27. Pettit P (2010) Current opinion: complications and troubleshooting of sacral neuromodulation. *Int Urogynecol J* 21 Suppl 2: S491-496.
28. Kanafani ZA, Dakdouki GK, El-Dbouni O, Bawwab T, Kanj SS (2006) Surgical site infections following spinal surgery at a tertiary care center in Lebanon: incidence, microbiology, and risk factors. *Scand J Infect Dis* 38: 589-592.
29. Kang BU, Lee SH, Ahn Y, Choi WC, Choi YG (2010) Surgical site infection in spinal surgery: detection and management based on serial C-reactive protein measurements. *J Neurosurg Spine* 13: 158-164.
30. Sierra-Hoffman M, Jinadatha C, Carpenter JL, Rahm M (2010) Postoperative instrumented spine infections: a retrospective review. *South Med J* 103: 25-30.
31. Owens CD, Stoessel K (2008) Surgical site infections: epidemiology, microbiology and prevention. *J Hosp Infect* 70 Suppl 2: 3-10.
32. Martone WJ, Nichols RL (2001) Recognition, prevention, surveillance, and management of surgical site infections: introduction to the problem and symposium overview. *Clin Infect Dis* 33 Suppl 2: S67-68.
33. CULBERTSON WR, ALTEMEIER WA, GONZALEZ LL, HILL EO (1961) Studies on the epidemiology of postoperative infection of clean operative wounds. *Ann Surg* 154: 599-610.
34. HOWE CW, MARSTON AT (1962) A study on sources of postoperative staphylococcal infection. *Surg Gynecol Obstet* 115: 266-275.
35. BURKE JF (1963) IDENTIFICATION OF THE SOURCES OF STAPHYLOCOCCI CONTAMINATING THE SURGICAL WOUND DURING OPERATION. *Ann Surg* 158: 898-904.
36. Aglietti P, Salvati EA, Wilson PD Jr, Kutner LJ (1974) Effect of a surgical horizontal unidirectional filtered air flow unit on wound bacterial contamination and wound healing. *Clin Orthop Relat Res* : 99-104.
37. Hamilton H, Jamieson J (2008) Deep infection in total hip arthroplasty. *Can J Surg* 51: 111-117.
38. Pryor F, Messmer PR (1998) The effect of traffic patterns in the OR on surgical site infections. *AORN J* 68: 649-660.
39. Stamm WE, Feeley JC, Facklam RR (1978) Wound infections due to group A streptococcus traced to a vaginal carrier. *J Infect Dis* 138: 287-292.
40. Hacek DM, Robb WJ, Paule SM, Kudrna JC, Stamos VP, et al. (2008) *Staphylococcus aureus* nasal decolonization in joint replacement surgery reduces infection. *Clin Orthop Relat Res* 466: 1349-1355.
41. Bode LG, Kluytmans JA, Wertheim HF, Bogaers D, Vandenbroucke-Grauls CM, et al. (2010) Preventing surgical-site infections in nasal carriers of *Staphylococcus aureus*. *N Engl J Med* 362: 9-17.
42. Ong KL, Lau E, Manley M, Kurtz SM (2008) Effect of procedure duration on total hip arthroplasty and total knee arthroplasty survivorship in the United States Medicare population. *J Arthroplasty* 23: 127-132.
43. Gastmeier P, Sohr D, Breier A, Behnke M, Geffers C (2011) Prolonged duration of operation: an indicator of complicated surgery or of surgical (mis) management? *Infection* 39: 211-215.
44. Bucher BT, Guth RM, Elward AM, Hamilton NA, Dillon PA, et al. (2011) Risk factors and outcomes of surgical site infection in children. *J Am Coll Surg* 212: 1033-1038.
45. Dalstrom DJ, Venkatarayappa I, Manternach AL, Palcic MS, Heyse BA, et al. (2008) Time-dependent contamination of opened sterile operating-room trays. *J Bone Joint Surg Am* 90: 1022-1025.
46. Watanabe M, Sakai D, Matsuyama D, Yamamoto Y, Sato M, et al. (2010) Risk factors for surgical site infection following spine surgery: efficacy of intraoperative saline irrigation. *J Neurosurg Spine* 12: 540-546.

47. Chiang HY, Steelman VM, Pottinger JM, Schlueter AJ, Diekema DJ, et al. (2011) Clinical significance of positive cranial bone flap cultures and associated risk of surgical site infection after craniotomies or craniectomies. *J Neurosurg* 114: 1746-1754.
48. Talbot TR1 (2005) Diabetes mellitus and cardiothoracic surgical site infections. *Am J Infect Control* 33: 353-359.
49. Latham R, Lancaster AD, Covington JF, Pirolo JS, Thomas CS Jr (2001) The association of diabetes and glucose control with surgical-site infections among cardiothoracic surgery patients. *Infect Control Hosp Epidemiol* 22: 607-612.
50. Hirsch IB, Paauw DS (1997) Diabetes management in special situations. *Endocrinol Metab Clin North Am* 26: 631-645.
51. Vriesendorp TM, Moréllis QJ, Devries JH, Legemate DA, Hoekstra JB (2004) Early post-operative glucose levels are an independent risk factor for infection after peripheral vascular surgery. A retrospective study. *Eur J Vasc Endovasc Surg* 28: 520-525.
52. Mehta SK, Breitbart EA, Berberian WS, Liporace FA, Lin SS (2010) Bone and wound healing in the diabetic patient. *Foot Ankle Clin* 15: 411-437.
53. Gibbs J, Cull W, Henderson W, Daley J, Hur K, et al. (1999) Preoperative serum albumin level as a predictor of operative mortality and morbidity: results from the National VA Surgical Risk Study. *Arch Surg* 134: 36-42.
54. Choban PS, Flancbaum L (1997) The impact of obesity on surgical outcomes: a review. *J Am Coll Surg* 185: 593-603.
55. Dindo D, Muller MK, Weber M, Clavien PA (2003) Obesity in general elective surgery. *Lancet* 361: 2032-2035.
56. Walid MS, Robinson JS 3rd, Robinson ER, Brannick BB, Ajjan M, et al. (2010) Comparison of outpatient and inpatient spine surgery patients with regards to obesity, comorbidities and readmission for infection. *J Clin Neurosci* 17: 1497-1498.
57. Bamgbade OA, Rutter TW, Nafiu OO, Dorje P (2007) Postoperative complications in obese and nonobese patients. *World J Surg* 31: 556-560.
58. Konishi T, Watanabe T, Kishimoto J, Nagawa H (2006) Elective colon and rectal surgery differ in risk factors for wound infection: results of prospective surveillance. *Ann Surg* 244: 758-763.
59. Busti AJ, Hooper JS, Amaya CJ, Kazi S (2005) Effects of perioperative antiinflammatory and immunomodulating therapy on surgical wound healing. *Pharmacotherapy* 25: 1566-1591.
60. Fortun J, Martin-Davila P, Pascual J, Cervera C, Moreno A, Gavalda J, et al. (2010) RESITRA Transplant Network. Immunosuppressive therapy and infection after kidney transplantation. *Transpl Infect Dis* 12: 397-405.
61. Handlin DS, Baker T (1992) The effects of smoking on postoperative recovery. *Am J Med* 93: 32S-37S.
62. Møller AM, Villebro N, Pedersen T, Tønnesen H (2002) Effect of preoperative smoking intervention on postoperative complications: a randomised clinical trial. *Lancet* 359: 114-117.
63. Myles PS, Iacono GA, Hunt JO, Fletcher H, Morris J, McLroy D, et al. (2002) Risk of respiratory complications and wound infection in patients undergoing ambulatory surgery: smokers versus nonsmokers. *Anesthesiology* 97: 842-847.
64. Thomsen T, Tønnesen H, Okholm M, Kroman N, Maibom A, et al. (2010) Brief smoking cessation intervention in relation to breast cancer surgery: a randomized controlled trial. *Nicotine Tob Res* 12: 1118-1124.
65. Nath B, Li Y, Carroll JE, Szabo G, Tseng JF, et al. (2010) Alcohol exposure as a risk factor for adverse outcomes in elective surgery. *J Gastrointest Surg* 14: 1732-1741.
66. Delgado-Rodríguez M, Mariscal-Ortiz M, Gómez-Ortega A, Martínez-Gallego G, Palma-Pérez S, Sillero-Arenas M, et al. (2003) Alcohol consumption and the risk of nosocomial infection in general surgery. *Br J Surg* 90: 1287-1293.
67. Valentine RJ, Weigelt JA, Dryer D, Rodgers C (1986) Effect of remote infections on clean wound infection rates. *Am J Infect Control* 14: 64-67.
68. Gupta K, Strymish J, Abi-Haidar Y, Williams SA, Itani KM, et al. (2011) Preoperative nasal methicillin-resistant *Staphylococcus aureus* status, surgical prophylaxis, and risk-adjusted postoperative outcomes in veterans. *Infect Control Hosp Epidemiol* 32: 791-796.
69. Vamvakas EC, Moore SB (1994) Blood transfusion and postoperative septic complications. *Transfusion* 34: 714-727.
70. Ismael H, Horst M, Farooq M, Jordon J, Patton JH, et al. (2011) Adverse effects of preoperative steroid use on surgical outcomes. *Am J Surg* 201: 305-308.
71. McIntyre FJ, McCloy R (1994) Shaving patients before operation: a dangerous myth? *Ann R Coll Surg Engl* 76: 3-4.
72. Kjønnesen I, Andersen BM, Søndena VG, Segadal L (2002) Preoperative hair removal—a systematic literature review. *AORN J* 75: 928-938, 940.
73. Alexander JW, Fischer JE, Boyajian M, Palmquist J, Morris MJ (1983) The influence of hair-removal methods on wound infections. *Arch Surg* 118: 347-352.
74. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR (1999) Guideline for prevention of surgical site infection, 1999. Hospital Infection Control Practices Advisory Committee. *Infect Control Hosp Epidemiol* 20: 250-278.
75. Webster J, Osborne S (2006) Meta-analysis of preoperative antiseptic bathing in the prevention of surgical site infection. *Br J Surg* 93: 1335-1341.
76. Maiwald M, Widmer AF, Rotter ML (2011) Lack of evidence for attributing chlorhexidine as the main active ingredient in skin antiseptics preventing surgical site infections. *Infect Control Hosp Epidemiol* 32: 404-405.
77. Lee I, Agarwal RK, Lee BY, Fishman NO, Umscheid CA (2010) Systematic review and cost analysis comparing use of chlorhexidine with use of iodine for preoperative skin antiseptics to prevent surgical site infection. *Infect Control Hosp Epidemiol* 31: 1219-1229.
78. Levin I, Amer-Alishiek J, Avni A, Lessing JB, Satel A, et al. (2011) Chlorhexidine and alcohol versus povidone-iodine for antiseptics in gynecological surgery. *J Womens Health (Larchmt)* 20: 321-324.
79. Darouiche RO, Wall MJ Jr, Itani KM, Otterson MF, Webb AL, et al. (2010) Chlorhexidine-Alcohol versus Povidone-Iodine for Surgical-Site Antisepsis. *N Engl J Med* 362: 18-26.
80. Epstein NE1 (2011) Preoperative, intraoperative, and postoperative measures to further reduce spinal infections. *Surg Neurol Int* 2: 17.
81. Rosenberger LH, Politano AD, Sawyer RG (2011) The surgical care improvement project and prevention of post-operative infection, including surgical site infection. *Surg Infect (Larchmt)* 12: 163-168.
82. Bratzler DW, Houck PM (2005) Surgical Infection Prevention Guideline Writers Workgroup. Antimicrobial prophylaxis for surgery: an advisory statement from the National Surgical Infection Prevention Project. *Am J Surg* 189: 395-404.
83. Guaschino S, De Santo D, De Seta F (2002) New perspectives in antibiotic prophylaxis for obstetric and gynaecological surgery. *J Hosp Infect* 50 Suppl A: S13-16.
84. Christian SS, Christian JS (1997) The cephalosporin antibiotics. *Prim Care Update Ob/Gyns* 4:168-174.
85. Kourbatova EV, Halvosa JS, King MD, Ray SM, White N, Blumberg HM, et al. (2005) Emergence of community-associated methicillin-resistant *Staphylococcus aureus* USA 300 clone as a cause of health care-associated infections among patients with prosthetic joint infections. *Am J Infect Control* 33: 385-391.
86. Chang S, Sievert DM, Hageman JC, Boulton ML, Tenover FC, Downes FP, et al. (2003) Vancomycin Resistant *Staphylococcus Aureus* Investigative Team. Infection with vancomycin-resistant *Staphylococcus aureus* containing the van: a resistance gene. *N Engl J Med* 348: 1342-1347.
87. Steinberg JP, Braun BI, Hellinger WC, Kusek L, Bozikis MR, Bush AJ, et al. (2009) Trial to Reduce Antimicrobial Prophylaxis Errors (TRAPE) Study Group. Timing of antimicrobial prophylaxis and the risk of surgical site infections: Results from the Trial to Reduce Antimicrobial Prophylaxis Errors (TRAPE). *Arch Surg* 250: 10-16.
88. Potenza B, Deligencia M, Estigoy B, Faraday E, Snyder A, Angle N, et al. (2009) Lessons learned from the institution of the Surgical Care Improvement Project at a teaching medical center. *Am J Surg* 198: 881-888.
89. Weber WP, Marti WR, Zwahlen M, Misteli H, Rosenthal R, et al. (2008) The timing of surgical antimicrobial prophylaxis. *Ann Surg* 247: 918-926.
90. van Kasteren ME, Manniën J, Ott A, Kullberg BJ, de Boer AS, et al. (2007) Antibiotic prophylaxis and the risk of surgical site infections following total hip arthroplasty: timely administration is the most important factor. *Clin Infect Dis* 44: 921-927.
91. Bratzler DW, Hunt DR (2006) The surgical infection prevention and surgical care improvement projects: national initiatives to improve outcomes for patients having surgery. *Clin Infect Dis* 43: 322-330.
92. Garey KW, Dao T, Chen H, Amrutkar P, Kumar N, et al. (2006) Timing of vancomycin prophylaxis for cardiac surgery patients and the risk of surgical site infections. *J Antimicrob Chemother* 58: 645-650.

93. Forse RA, Karam B, MacLean LD, Christou NV (1989) Antibiotic prophylaxis for surgery in morbidly obese patients. *Surgery* 106: 750-756.
94. Edmiston CE, Krepel C, Kelly H, Larson J, Andris D, et al. (2004) Perioperative antibiotic prophylaxis in the gastric bypass patient: do we achieve therapeutic levels? *Surgery* 136: 738-747.
95. Kanayama M, Hashimoto T, Shigenobu K, Oha F, Togawa D, et al. (2007) Effective prevention of surgical site infection using a Centers for Disease Control and Prevention guideline-based antimicrobial prophylaxis in lumbar spine surgery. *J Neurosurg Spine* 6: 327-329.
96. Harbarth S, Samore MH, Lichtenberg D, Carmeli Y (2000) Prolonged antibiotic prophylaxis after cardiovascular surgery and its effect on surgical site infections and antimicrobial resistance. *Circulation* 101: 2916-2921.
97. Dellinger EP, Gross PA, Barrett TL, Krause PJ, Martone WJ, McGowan JE Jr, et al. (1994) Quality standard for antimicrobial prophylaxis in surgical procedures. The Infectious Diseases Society of America. *Infect Control Hosp Epidemiol* 15: 182-188.
98. Groenewold MD, Gribnau AJ, Ubbink DT (2011) Topical haemostatic agents for skin wounds: a systematic review. *BMC Surg* 11: 15.
99. Davies B, Guyuron B, Husami T (1991) The role of lidocaine, epinephrine, and flap elevation in wound healing after chemical peel. *Ann Plast Surg* 26: 273-278.
100. Wakamatsu T1 (1992) [Effects of local anesthetics on healing process of extraction wound in rats with reference to effects of epinephrine]. *Kokubyo Gakkai Zasshi* 59: 613-630.
101. Parr AM, Zoutman DE, Davidson JS (1999) Antimicrobial activity of lidocaine against bacteria associated with nosocomial wound infection. *Ann Plast Surg* 43: 239-245.
102. Stratford AF, Zoutman DE, Davidson JS (2002) Effect of lidocaine and epinephrine on *Staphylococcus aureus* in a guinea pig model of surgical wound infection. *Plast Reconstr Surg* 110: 1275-1279.
103. Sivamani RK, Pullar CE, Manabat-Hidalgo CG, Rocke DM, Carlsen RC, et al. (2009) Stress-mediated increases in systemic and local epinephrine impair skin wound healing: potential new indication for beta blockers. *PLoS Med* 6: e12.
104. Romana-Souza B, Otranto M, Vieira AM, Filgueiras CC, Fierro IM, et al. (2010) Rotational stress-induced increase in epinephrine levels delays cutaneous wound healing in mice. *Brain Behav Immun* 24: 427-437.
105. Rodrigues FV, Hochman B, Wood VT, Simões MJ, Juliano Y, et al. (2011) Effects of lidocaine with epinephrine or with buffer on wound healing in rat skin. *Wound Repair Regen* 19: 223-228.
106. Lord JW, Rossi G, Daliana M (1977) Intraoperative antibiotic wound lavage: an attempt to eliminate postoperative infection in arterial and clean general surgical procedures. *Ann Surg* 185: 634-641.
107. Sookpotarom P, Khampiwmar W, Termwattanaphakdee T (2010) Vigorous wound irrigation followed by subcuticular skin closure in children with perforated appendicitis. *J Med Assoc Thai* 93: 318-323.
108. Hayashi T, Shirane R, Yokosawa M, Kimiwada T, Tominaga T (2010) Efficacy of intraoperative irrigation with saline for preventing shunt infection. *J Neurosurg Pediatr* 6: 273-276.
109. Savitz SI, Savitz MH, Goldstein HB, Mouracade CT, Malangone S (1998) Topical irrigation with polymyxin and bacitracin for spinal surgery. *Surg Neurol* 50: 208-212.
110. Gallup DC, Gallup DG, Nolan TE, Smith RP, Messing MF, et al. (1996) Use of a subcutaneous closed drainage system and antibiotics in obese gynecologic patients. *Am J Obstet Gynecol* 175: 358-361.
111. Pfeiffer P, Jørgensen S, Kristiansen TB, Jørgensen A, Hölmich LR (2009) Protective effect of topical antibiotics in breast augmentation. *Plast Reconstr Surg* 124: 629-634.
112. Bergamini TM, Lamont PM, Cheadle WG, Polk HC Jr (1984) Combined topical and systemic antibiotic prophylaxis in experimental wound infection. *Am J Surg* 147: 753-756.
113. Dirschl DR, Wilson FC (1991) Topical antibiotic irrigation in the prophylaxis of operative wound infections in orthopedic surgery. *Orthop Clin North Am* 22: 419-426.
114. Owens BD, Wenke JC (2007) Early wound irrigation improves the ability to remove bacteria. *J Bone Joint Surg Am* 89: 1723-1726.
115. Winingner DA, Fass RJ (1996) Antibiotic-impregnated cement and beads for orthopedic infections. *Antimicrob Agents Chemother* 40: 2675-2679.
116. Bourne RB (2004) Prophylactic use of antibiotic bone cement: an emerging standard—in the affirmative. *J Arthroplasty* 19: 69-72.
117. Hanssen AD (2004) Prophylactic use of antibiotic bone cement: an emerging standard—in opposition. *J Arthroplasty* 19: 73-77.
118. Maurice-Williams RS, Pollock J (1999) Topical antibiotics in neurosurgery: a re-evaluation of the Malis technique. *Br J Neurosurg* 13: 312-315.
119. Freiler JF, Steel KE, Hagan LL, Rathkopf MM, Roman-Gonzalez J (2005) Intraoperative anaphylaxis to bacitracin during pacemaker change and laser lead extraction. *Ann Allergy Asthma Immunol* 95: 389-393.
120. Damm S (2011) Intraoperative anaphylaxis associated with bacitracin irrigation. *Am J Health Syst Pharm* 68: 323-327.
121. Moucha CS, Clyburn TA, Evans RP, Prokuski L (2011) Modifiable risk factors for surgical site infection. *Instr Course Lect* 60: 557-564.
122. Dellinger EP (2005) Increasing inspired oxygen to decrease surgical site infection: time to shift the quality improvement research paradigm. *JAMA* 294: 2091-2092.
123. Greif R, Akca O, Horn EP, Kurz A, Sessler DI, et al. (2000) Outcome Research Group. Supplemental perioperative oxygen to reduce the incidence of surgical-wound infection. *N Engl J Med* 342: 161-167.
124. Kurz A, Sessler DI, Lenhardt R (1996) Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. Study of Wound Infection and Temperature Group. *N Engl J Med* 334: 1209-1215.
125. Gosain A, Gamelli RL, DiPietro LA (2009) Norepinephrine-mediated suppression of phagocytosis by wound neutrophils. *J Surg Res* 152: 311-318.
126. Postlethwaite RW (1981) Principles of operative surgery: Antisepsis, technique, sutures, and drains. In: Sabiston DC (ed). *Davis-Christopher Textbook of Surgery*. Philadelphia: WB Saunders: 322.
127. Kaafarani HM, Kaufman D, Reda D, Itani KM (2010) Predictors of surgical site infection in laparoscopic and open ventral incisional herniorrhaphy. *J Surg Res* 163: 229-234.
128. Soballe PW, Nimbkar NV, Hayward I, Nielsen TB, Drucker WR (1998) Electric cautery lowers the contamination threshold for infection of laparotomies. *Am J Surg* 175: 263-266.
129. Yilmaz KB, Dogan L, Nalbant H, Akinci M, Karaman N, Ozaslan C, et al. (2011) Comparing scalpel, electrocautery and ultrasonic dissector effects: the impact on wound complications and pro-inflammatory cytokine levels in wound fluid from mastectomy patients. *J Breast Cancer* 14: 58-63.
130. Parlakgumus A, Ezer A, Caliskan K, Emeksiz S, Karakaya J, Colakoglu T, et al. (2011) Effects of a tissue sealing-cutting device versus monopolar electrocautery on early pilonidal wound healing: a prospective randomized controlled trial. *Dis Colon Rectum* 54: 1155-1161.
131. Dye ES, Kapral FA (1980) Partial characterization of a bactericidal system in staphylococcal abscesses. *Infect Immun* 30: 198-203.
132. McGeehan D, Hunt D, Chaudhuri A, Rutter P (1980) An experimental study of the relationship between synergistic wound sepsis and suture materials. *Br J Surg* 67: 636-638.
133. Smith TO, Sexton D, Mann C, Donell S (2010) Sutures versus staples for skin closure in orthopaedic surgery: meta-analysis. *BMJ* 340: c1199.
134. Millbourn D, Cengiz Y, Israelsson LA (2011) Risk factors for wound complications in midline abdominal incisions related to the size of stitches. *Hernia* 15: 261-266.