INTRODUCTION

Surgical site infections (SSIs) have played a major role in the evolution of medical care throughout history. Wound complications contributed significantly to the historical surgical mortality rates before the development of Lister’s aseptic approach in the nineteenth century. The impact of the antiseptic/aseptic techniques was readily apparent in its adaptation to battlefield medicine. During the Civil War in America, surgeons routinely operated bare-handed, with wound suppuration considered to be a beneficial aspect of wound healing. With the gradual acceptance of the principles of antisepsis, and the usage of sterile dressings and aseptic surgical technique, there was a dramatic reduction in mortality from wounds to 7.4% in the Spanish-American War.

Despite nearly 2 centuries of medical progress, the management of surgical infection remains a pressing concern, and SSIs continue to be a leading component of nosocomial morbidity and mortality. In this article, the epidemiology, pathogenesis,
risk factors, and approach to prevention of SSIs are reviewed. This review highlights the multifaceted and multidisciplinary approach to management of SSIs, which are a critical aspect of infection control outcomes.

**DEFINITIONS**

To assist with appropriate surveillance of SSIs, establishing clear definitions for cases of SSIs was critical. The Centers for Disease Control and Prevention (CDC) established the National Healthcare Safety Network (NHSN) to monitor quality control measures, including SSIs, and has defined widely used definitions for SSI (Box 1). SSI are classified based on the depth of involvement of the infection, which may be confined to the skin and subcutaneous tissues (superficial incisional SSI), involve the deep soft tissue, such as the fascial and muscular layers (deep incisional SSI), or extend further beyond these anatomic boundaries (organ/space SSI) (Fig. 1). Incisional SSIs are further subdivided into primary and secondary for cases with more than one incision. For instance, a primary incisional SSI involves the primary incision (eg, chest incision for coronary artery bypass grafting), and a secondary incisional SSI involves secondary incisions (eg, leg incision for donor site in coronary artery bypass grafting).

**EPIDEMIOLOGY**

Recognizing the historical context of surgical infection can highlight the gains that have been made over the past few centuries. Before the antisepsis era, the risk of surgery was exceedingly high due to the enormous rates of surgical infection. Compounded by the absence of the effective anesthesia, early surgical procedures had limited success compared with the modern era. Acknowledgment of the aseptic approach made a significant impact on outcomes. The simple introduction of hand washing by Semmelweis resulted in a decrease in mortality due to puerperal sepsis from 12% to 2%. The development of multiple aspects of modern surgical care has led to significant improvements in the historical context described. Nevertheless, SSIs remain a frequent postoperative complication, developing in 3% to 20% of surgical procedures. The rate of SSI is highly variable depending on the specific operative procedure, with rates that can be even higher depending on the number of risk factors present.

There is a substantial impact of SSI on both morbidity and mortality. However, establishing the exact impact of SSI is difficult because of the dependence on accuracy of reporting and the variability of patient follow-up. In the 1980s, it was observed that SSI led to a 10-day increase in hospital length of stay. Even a decade later, another study reported persistent delayed discharge from hospital and increased requirement for post-discharge care. In a study of 288,906 patients, in-hospital mortality for the patients with SSIs was 14.5% versus 1.8% of patients with no SSI. SSIs are estimated to be responsible for more than 8000 deaths annually in the United States. SSIs may be of even greater consequence in developing countries, because surveillance rates of SSI in a study conducted by the International Nosocomial Infection Control Consortium were higher for most surgical procedures compared with CDC-NHSN rates.

**RISK FACTORS FOR SURGICAL SITE INFECTION**

From a general perspective, the microbes responsible for infection of surgical wounds originate from either the surrounding skin or associated structures that are contiguous
### Box 1
Centers for Disease Control and Prevention–National Healthcare Safety Network definitions for surgical site infections

**Superficial incisional surgical site infection**
Infection occurs within 30 days after the operative procedure and
Involves only skin and subcutaneous tissue of the incision and
Patient has at least 1 of the following:

a. Purulent drainage from the superficial incision

b. Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision

c. At least 1 of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness, or heat, and superficial incision is deliberately opened by surgeon and is culture positive or not cultured. A culture-negative finding does not meet this criterion

d. Diagnosis of superficial incisional SSI by the surgeon or attending physician

**Deep incisional surgical site infection**
Infection occurs within 30 days after the operative procedure if no implant is left in place or within 1 year if implant is in place and the infection appears to be related to the operative procedure and
Involves deep soft tissues (eg, fascial and muscle layers) of the incision and
Patient has at least 1 of the following:

a. Purulent drainage from the deep incision but not from the organ/space component of the surgical site

b. A deep incision spontaneously dehisces or is deliberately opened by a surgeon and is culture-positive or not cultured when the patient has at least 1 of the following signs or symptoms: fever (>38°C or localized pain or tenderness. A culture-negative finding does not meet this criterion

c. An abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination

d. Diagnosis of a deep incisional SSI by a surgeon or attending physician

**Organ/space surgical site infection**
Infection occurs within 30 days after the operative procedure if no implant is left in place or within 1 year if implant is in place and the infection appears to be related to the operative procedure and infection involves any part of the body, excluding the skin incision, fascia, or muscle layers, that is opened or manipulated during the operative procedure and
Patient has at least 1 of the following:

a. Purulent drainage from a drain that is placed through a stab wound into the organ/space

b. Organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space

c. An abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation, or by histopathologic or radiologic examination

d. Diagnosis of an organ/space SSI by a surgeon or attending physician.

*From* Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. *Am J Infect Control* 2008;36:313–4; with permission.
with the regions of the surgical procedure. The logical extension of this principle is that the risk of wound contamination and subsequent SSI depends on location, the nature of the surgical wound/incision, and the procedure performed. The CDC wound classification system defines wound class based on risk and is divided into 4 categories: clean, clean-contaminated, contaminated, and dirty (Table 1). With clean wounds, the expected risk is from microbes located directly on the surface of the skin, or introduced from the external environment. With increasing wound class, there is increased exposure to microorganisms that are present on internal structures of the body, such as epithelial surfaces of the gastrointestinal tract and genitourinary tract. In the early epidemiologic studies, the SSI rate increased with wound class (I, 2.1%; II, 3.3%; III, 6.4%; IV, 7.1%).

Appropriate risk stratification for SSI cannot be limited to the wound alone. There are a variety of patient-related factors and perioperative factors that can significantly affect the risk of SSI in a surgical patient (Box 2). One system of risk stratification is the National Nosocomial Infection Surveillance (NNIS) System risk score, based on 3 factors. These factors are (1) an American Society of Anesthesiology preoperative assessment score of greater than or equal to 3; (2) an operation with a wound classification as contaminated or dirty; and (3) an operation longer than the 75th percentile in duration for the specific procedure. In the original development of the NNIS risk score, each additional risk factor resulted in increasing rates of SSI, even within the same traditional wound class. In the most recent publication of aggregate data from the NHSN SSI surveillance system, the effects of risk factors remain apparent (Table 2), with escalating SSI rates with the number of risk factors. The NNIS score has been further modified to account for some specific instances of laparoscopic cases, as the risk for SSI can be lower.

The risk factors identified in the NNIS risk scoring system are useful from surveillance and monitoring perspectives. However, prevention requires identification of
risk factors that are more readily modifiable than those listed in the NNIS scoring system. An approach to the risk factors of SSIs can be categorized into a schematic of microbial factors, patient factors, and perioperative factors.

MICROBIAL FACTORS

The predominant source of microbes involved in SSIs originate from either the skin or the surrounding tissues of the incision, or from deeper structures involved in the operative procedure (eg, enteric organisms in bowel-related surgeries). In the most recent NHSN surveillance report on 21,100 isolates from 2009 to 2010, the most frequently identified pathogens were, in order, *Staphylococcus aureus*, *Coagulase-negative Staphylococci*, *Escherichia coli*, *Enterococcus faecalis*, and *Pseudomonas aeruginosa*.12 The overall distribution of pathogens associated with SSI has changed to some extent over the past couple decades (Table 3).12–14 The proportion of gram-negative bacilli has decreased coinciding with a relative increase in the proportion of *S aureus*-related infection. In the most recently published 2010 NHSN data, *S aureus* accounted for 30.4% of SSI, up from 20% in the early 1990s. Individual institutions may have variations in the proportions of specific species, due to differences in the volumes of various surgical specialties.

The temporal trend of significance is the substantial growth in multidrug resistance (MDR). The most apparent example is the increase in methicillin-resistant *Staphylococcus aureus* (MRSA).15 In a study of community hospitals in southeastern United States, the incidence of MRSA-associated SSI increased from 12% in 2000 to 23% in 2005.16 In the 2010 NHSN update, the proportion of SSI due to MRSA was 43.7%.12 Increases in MRSA prevalence internationally show similar temporal trends.

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Table 1
Surgical wound classification

<table>
<thead>
<tr>
<th>Class</th>
<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Clean</td>
<td>An uninfected operative wound in which no inflammation is encountered and the respiratory, alimentary, genital, or uninfected urinary tract is not entered. In addition, clean wounds are primarily closed and, if necessary, drained with closed drainage. Operative incisional wounds that follow nonpenetrating (blunt) trauma should be included in this category if they meet the criteria.</td>
</tr>
<tr>
<td>II</td>
<td>Clean—contaminated</td>
<td>An operative wound in which the respiratory, alimentary, genital, or urinary tracts are entered under controlled conditions and without unusual contamination. Specifically, operations involving the biliary tract, appendix, vagina, and oropharynx are included in this category, provided no evidence of infection or major break in technique is encountered.</td>
</tr>
<tr>
<td>III</td>
<td>Contaminated</td>
<td>Open, fresh, accidental wounds. In addition, operations with major breaks in sterile technique (eg, open cardiac massage) or gross spillage from the gastrointestinal tract, and incisions in which acute, nonpurulent inflammation is encountered are included in this category.</td>
</tr>
<tr>
<td>IV</td>
<td>Dirty—infected</td>
<td>Old traumatic wounds with retained devitalized tissue and those that involve existing clinical infection or perforated visera. This definition suggests that the organisms causing postoperative infection were present in the operative field before the operation.</td>
</tr>
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</table>

In a Japanese study of 702 isolates, methicillin resistance in *S aureus* isolates was 72.0%. Community-acquired MRSA is increasing in prevalence, with the prevalence of nasal colonization with MRSA in the general population increasing from 0.8% to 1.5% from 2001–2002 to 2003–2004. Studies have attempted to clarify the relationship between colonization and risk for MRSA SSI. In a study of 9006 patients in a Pennsylvania tertiary care hospital by Kalra and colleagues, 4.3% of patients were positive for nasal MRSA screening; the MRSA SSI rate was 1.86% in MRSA-screen-positive patients compared with 0.20% in MRSA-screen-negative patients.

An important aspect of the temporal changes in MDR pathogens is the significant alteration in the pharmacodynamics of the antibiotics used to manage these infections. Several studies have shown an upward shift in minimal inhibitory concentration (MIC) of vancomycin in clinically isolated strains of MRSA, described as “MIC creep.”

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**Box 2**

**Risk factors for surgical site infection**

<table>
<thead>
<tr>
<th>Patient factors</th>
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<tbody>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Nutritional status</td>
</tr>
<tr>
<td>Diabetes</td>
</tr>
<tr>
<td>Smoking</td>
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<tr>
<td>Obesity</td>
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<tr>
<td>Coexistent infections at a remote body site</td>
</tr>
<tr>
<td>Colonization with microorganisms</td>
</tr>
<tr>
<td>Altered immune response</td>
</tr>
<tr>
<td>Length of preoperative stay</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Operative factors</th>
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<tbody>
<tr>
<td>Duration of surgical scrub</td>
</tr>
<tr>
<td>Skin antisepsis</td>
</tr>
<tr>
<td>Preoperative shaving</td>
</tr>
<tr>
<td>Preoperative skin preparation</td>
</tr>
<tr>
<td>Duration of operation</td>
</tr>
<tr>
<td>Antimicrobial prophylaxis</td>
</tr>
<tr>
<td>Operating room ventilation</td>
</tr>
<tr>
<td>Inadequate sterilization of instruments</td>
</tr>
<tr>
<td>Foreign material in the surgical site</td>
</tr>
<tr>
<td>Surgical drains</td>
</tr>
<tr>
<td>Surgical technique</td>
</tr>
<tr>
<td>Poor hemostasis</td>
</tr>
<tr>
<td>Failure to obliterate dead space</td>
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<tr>
<td>Tissue trauma</td>
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</tbody>
</table>

During a period between 2000 and 2004, Wang and colleagues\(^20\) reported on 6003 clinical isolates, showing a large significant increase in the proportion of isolates with vancomycin MIC of 1 mg/L from 19.9% to 70.4%. In a 5-year period between 2001 and 2005, Steinkraus and colleagues\(^21\) reported a significant increase in the MIC of vancomycin, oxacillin, and linezolid in 662 isolates collected over the 5-year period. For vancomycin, in particular, there was a significant shift in proportion of isolates with MIC \(\leq 0.5\) mg/L, from 46% in 2001 to 5% in 2006.

There have been conflicting data with respect to “MIC creep.” Several surveillance studies from Canadian, United Kingdom, and American centers have not demonstrated the same degree of MIC creep.\(^{22–24}\) Additional controversy lies in the methodologies to represent changes in MIC. In general, these trends remain cause for concern as higher MIC is predictive of vancomycin treatment failure in MRSA.\(^25\) In some series, MRSA infection has been independently associated with mortality.\(^26\) Narrowing of the therapeutic window will increase the risk for adverse effects as dosing targets are adjusted.\(^27\) Management of MRSA as a single example of antibiotic resistance carries a significant burden of cost.

### Table 2

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Risk Index (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CABG with chest and donor incision</td>
<td>0.35 2.55 4.26 8.49</td>
</tr>
<tr>
<td>Breast surgery</td>
<td>0.95 2.95 6.46</td>
</tr>
<tr>
<td>Colon surgery</td>
<td>3.99 5.59 7.06 9.47</td>
</tr>
<tr>
<td>Gallbladder surgery (inpatient)</td>
<td>0.23 0.61 1.72</td>
</tr>
<tr>
<td>Herniorrhaphy (inpatient)</td>
<td>0.74 2.42 5.25</td>
</tr>
<tr>
<td>Rectal surgery</td>
<td>3.47 7.99 26.67</td>
</tr>
<tr>
<td>Small bowel surgery</td>
<td>3.44 6.75 2.04</td>
</tr>
<tr>
<td>Thoracic surgery</td>
<td>0.76</td>
</tr>
</tbody>
</table>

*Abbreviation: CABG, coronary artery bypass grafting.*


### Table 3

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>S aureus</td>
<td>20%</td>
</tr>
<tr>
<td>Coagulase-negative Staphylococcus</td>
<td>14%</td>
</tr>
<tr>
<td>Enterococcus sp.</td>
<td>12%</td>
</tr>
<tr>
<td>E coli</td>
<td>8%</td>
</tr>
<tr>
<td>P aeruginosa</td>
<td>8%</td>
</tr>
<tr>
<td>Enterobacter sp</td>
<td>7%</td>
</tr>
<tr>
<td>K pneumoniae</td>
<td>3%</td>
</tr>
</tbody>
</table>

*Data from Refs.\(^{12–14}\)*
The concerns of antibiotic resistance are increasing as new mechanisms for multidrug resistance are continuing to develop. For instance, New Delhi metallo-β-lactamase 1 (NDM-1) was first reported in Sweden in 2008. It has been increasingly identified in isolates from India, Pakistan, and the United Kingdom. The global spread of NDM-1 is now broad, with identification in Canada, United States, Australia, China, and Russia. The resistance mechanism was first identified in *Klebsiella pneumoniae* and *E coli*. Other species of *Enterobacteriaceae* have now also been identified to harbor NDM-1, including *Acinetobacter, Enterobacter, Providencia,* and *Raoultella*. It has been primarily identified in patients with community-acquired pneumonia, urinary tract infections, and bacteremia. Nevertheless, like the spread geographically and in specification, there is significant potential impact with SSI. In one case report, *Acinetobacter baumanii* expressing NDM-1 was isolated from a Dacron graft infection. NDM-1 is just one example of an MDR mechanism that has spread globally in a few short years.

A discussion on microbial factors in surgical infection can extend far beyond a discussion on cause alone. There is a growing body of research literature that suggests that there is an important role of the host microbiome in response to disease. The most well-studied interactions are within inflammatory bowel disease, which demonstrates a clear relationship with altered microbiome composition. Understanding of the interaction of the host microbiome with wound healing is evolving. As an example, in an animal model of anastomotic leak, there is an association of anastomotic leak with specific virulence factors in *P aeruginosa*. Further research may significantly alter the understanding of surgical infection and the interaction with microbial etiologies.

**PATIENT FACTORS**

Patient comorbidities can contribute significantly to the potential risk of SSIs. These factors include age, obesity, smoking, diabetes mellitus, malnutrition, dyslipidemia, and immunosuppression (see Box 2). These factors are not directly accounted for in the NNIS classification scheme but can contribute significantly to the risk of SSI. Identification of these risk factors with appropriate preoperative history and physical examination is critical. The core principle for management of these patient-related risk factors is preoperative optimization.

Because many of the patient comorbidities are nonmodifiable, there can be a substantial increase in SSI risk. Particularly in urgent or emergent situations, there may not be an opportunity to optimize a patient’s comorbid status fully. The rate of SSI is expected to be much higher in emergency surgery, as opposed to elective cases, which has been demonstrated in many studies. The higher SSI rate in emergency cases also signifies patients that are more critically ill, with greater physiologic compromise, and expectedly, worse outcome.

Other patient-related risk factors are also often nonmodifiable in the timeline of preoperative planning. Although age is clearly a nonmodifiable risk factor, other comorbidities, such as diabetes, obesity, and immunosuppression, are not easily reversible in a short-term time frame. Optimization of these risk factors is critical. For diabetes, optimization of glucose control has been clearly demonstrated to have efficacy in reduction of SSI rates. In the cardiac surgery literature, rates of sternal wound infection have been shown to improve with the quality of glycemic control. Glycemic control optimization recommendations include a reduction in serum glucose levels and a reduction in HgbA1c to less than 7.0%.

Smoking results in significantly increased risk of SSI because of its effects on local tissue perfusion. Large numbers of studies have consistently shown that smoking
results in at least a 2-fold increased risk of SSI. In one trial by Møller and colleagues of 120 patients, smoking cessation therapy resulted in a reduction of wound-related complications from 31% to 5%. This finding has been confirmed by additional studies, and in meta-analyses of trial data. Recommendations are for smoking cessation at least 30 days before operation. For patients that have significantly elevated risk because of risk factors that cannot be modified, additional preventative measures need to be considered and can include the use of altered protocols for antimicrobial prophylaxis (as discussed later), or consideration of additional risk reduction measures.

PERIOPERATIVE FACTORS

Preventative measures in the preoperative period have changed rapidly over the past few decades. A large volume of research has established the importance of a host of preventative measures in the operative period. Examples include skin decontamination, perioperative warming, and antimicrobial prophylaxis. As additional studies have been conducted with increasing methodological rigor, from observational studies to randomized controlled trials, refinements of existing preventative measures have further improved the efficacy of these measures. This review focuses on areas of prevention that are the focus of significant active research or have seen recent changes in key guidelines or recommendations.

Skin Decontamination

The use of antiseptic agents topically has long been recommended for use in skin decontamination. The 2 broad classes of topical agents include chlorhexidine-based preparations and iodophor-based agents. In addition, these agents can be combined with isopropyl alcohol (IPA) in solution. Several studies have sought to address potential differences in efficacy between the various available agents, although there has been significant inconsistency of results, which have been also been confounded by methodological differences between the studies.

In the systematic review and meta-analysis conducted by Lee and colleagues, chlorhexidine-based agents were found to reduce the risk of SSIs significantly, with an adjusted risk ratio of 0.64, and result in a net cost-savings over the use of iodophor-based agents. This analysis included 9 randomized controlled trials, but in several of the included trials, chlorhexidine-based solutions containing IPA were compared with povidone-iodine solutions not containing IPA, which confounded the results of the analysis. In a nonrandomized study by Swenson and colleagues, there was no significant difference between chlorhexidine/IPA and 1 of 2 forms of iodophor-based agents (povidone-iodine or iodine povacrylex in IPA).

In the most recently published cohort study by Hakkarainen and colleagues, there were no significant differences between 4 different preparations of skin antisepsis agents (chlorhexidine/IPA, chlorhexidine, povidone-iodine, and iodine-povacrylex/IPA) in a cohort of primarily clean-contaminated general surgical cases. In their conclusion, there was minimal incremental benefit for chlorhexidine-based agent in their specific subset of clean-contaminated cases. As one prospective European study highlighted, there was no direct correlation between the residual bacterial flora following disinfection and subsequent SSI in a variety of surgical cases, suggesting that in certain surgical disciplines, the choice of skin antisepsis has less effect, particularly when the microbial cause lies in noncutaneous sources, such as enteric sources for general surgical procedures.
Antibiotic Prophylaxis

From a historical perspective, routine antibiotic prophylaxis was questioned for its usefulness. With demonstrated clinical benefit in the clinical trials conducted separately by Polk and Lopez-Mayor and Stone and colleagues, there has been tremendous improvement in SSI as an outcome. From the outset, the development of antibiotic prophylaxis has undoubtedly led to a clear reduction in rates of SSI. The complexity and nuance of clinical practice guidelines has continued to become more complex and refined.

Although there have been continual updates to the clinical practice guidelines, the general principles of antimicrobial prophylaxis are consistent. First, the antimicrobial agent should be safe. Second, an appropriate antimicrobial agent should be selected that has a narrow spectrum of coverage for the expected relevant pathogens. Third, antimicrobial prophylaxis should be administered in the preoperative period to allow serum and tissue concentrations to reach appropriate levels at the time of incision. Last, the antimicrobial agent should be administered for the shortest effect period, with appropriate discontinuation of the agent.

Clinical practice guidelines for antimicrobial prophylaxis were recently updated in 2013 in a joint publication by the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, the Surgical Infection Society, and the Society for Healthcare Epidemiology of America. The revised guidelines replaced the previously published 1999 guidelines and highlighted several focuses including timing of preoperative dosing, weight-based dosing, and duration of postoperative prophylaxis.

Selection of antibiotics for prophylaxis should be made with the primary consideration of the spectrum of coverage required. This consideration should be made because of the wound classification and the overall risk of infection. For example, in clean surgical procedures, the risk of SSI is relatively low and, in several cases, antimicrobial prophylaxis is not indicated. Prophylaxis is considered in specific clean procedures where the consequence of infection is critical (eg, prosthetic implants, cardiac pacemakers). Consideration of intrinsic patient-related factors associated with increased risk of SSI (eg, age, malnutrition, immunosuppression) is relevant and appropriate justification for the use of antimicrobial prophylaxis.

A meta-analysis conducted by Bowater and colleagues demonstrated that the relative risk reduction was the same across wound classes.

In clean procedures, the primary coverage is for the likely Staphylococcus sp. that will be the predominant cause. For clean-contaminated procedures, similar spectrum of coverage for Staphylococcus sp. is required, with additional coverage as needed depending on the site of surgery. As such, first-generation and second-generation cephalosporins remain the recommended prophylactic antibiotics for a large number of surgical procedures. For contaminated and dirty wound classes, prophylaxis is typically not indicated, because therapeutic antibiotic management is required.

Preoperative dosing of antibiotic prophylaxis is optimized to allow serum and tissue concentrations to reach sufficient levels at the time of incision. Several studies have studied the precise timeline for preoperative administration of prophylaxis to achieve maximal benefit. In 1992, Classen and colleagues showed a decreased SSI rate to 0.59% with administration within 2 hours of incision, compared with 3.8% for early (2–24 hours before incision) and 3.3% for postoperative administration. In a cardiac surgery study of 2048 patients, the rate of SSI was lowest in the group receiving vancomycin prophylaxis in the window of 16 to 60 minutes before incision.

Trends have been seen in several studies that may suggest that the window for preoperative antibiotics could be narrowed to 30 minutes of incision. In the Trial to
Reduce Antimicrobial Prophylaxis Errors (TRAPE) study of 4722 patients undergoing cardiac, arthroplasty, or hysterectomy procedures, the effect of specific windows of antibiotic prophylaxis (in 30-minute intervals, preceding and following incision) was examined.69 The lowest rate of SSI was in the 30-minute window immediately before incision. In an orthopedic study by van Kasteren and colleagues,70 1922 patients undergoing hip arthroplasty were examined. The rates of SSI in the groups receiving antibiotics in the 1- to 30-minute and 31- to 60-minute windows were 2.19% and 2.60%, respectively, which was not statistically significant. Both studies reinforced that the highest rate of SSI occurred in groups receiving antibiotics following incision. The potential incremental benefit of an earlier antibiotic window is likely small and would be difficult to detect without significantly larger sample sizes. Current guidelines emphasize prophylaxis administration within 60 minutes of incision, or within 120 minutes for antibiotics requiring longer infusion times.63

In the updated clinical practice guidelines, weight-based dosing is an additional focus.63 Particularly in obese patients, studies have shown the pharmacokinetics of antibiotic administration are significantly altered. In a 1989 study on obese patients undergoing gastoplasty and normal-weight adults undergoing abdominal surgery, 1 g dosing of cefazolin resulted in significantly lower blood and tissue concentrations in obese patients.71 However, 2 g dosing of cefazolin resulted in blood and tissue levels equivalent to normal-weight patients. Guidelines recommend increased dosing and fewer adjustments in renal impairment.63,64

Adequate redosing of antibiotics for longer operative procedures is necessary for risk reduction. With longer procedures, serum and tissue concentrations can drop below adequate levels, particularly in antibiotics with shorter half-lives (eg, cefazolin, cefoxitin, gentamicin).63,72 The effect was seen even in smaller case series. In the study by Morita and colleagues73 of 131 patients undergoing colorectal procedures, the SSI rates in procedures longer than 4 hours were 8.5% and 26.5%, in groups with or without redosing, respectively. In the TRAPE trial, the rate of SSI was increased with an absence of redosing, 5.5% versus 1.8%.69 Guidelines emphasize repeated dosing at intervals of 2 half-lives of the antibiotic used.63

Additional routes of antibiotic administration have been investigated in the past and have been historically ruled out. Topical routes of antibiotic prophylaxis have been considered for some time. Recent reinvestigation into topical antibiotic prophylaxis has been most thorough in the cardiac surgery literature. Gentamicin-impregnated sponges have been studied in several randomized controlled trials for the prevention of sternal wounds.74–77 A recent meta-analysis by Mavros and colleagues78 demonstrated that gentamicin collagen sponges reduced the risk of deep sternal wound infections, although there was significant heterogeneity among the included randomized controlled trials. However, in a trial by Bennett-Guerrero and colleagues,79 no benefit was seen in a group of 602 colorectal surgery patients, with significantly higher SSI rates in the gentamicin sponge group. Further interest is still present in examining topical antibiotics in general surgical populations,80 but more rigorous evidence will need to be presented before any adoption. With the recent guidelines, there are no recommendations describing a role for topical routes of antibiotic administration.63

Additional Measures

Several additional measures have been investigated for implementation in the prevention of SSI. In many circumstances, recommendations have been equivocal due to the lack of evidence or the presence of often contradictory evidence. In these cases, guidelines are directed by expert opinion and experience. Further research is
continuing to clarify controversial issues in SSI prevention, and in some cases, causing further controversy.

As a prime example, perioperative oxygenation was shown in 2 early trials to lead to a reduction in SSI rates with the use of 80% oxygen intraoperatively and immediately postoperatively. Further investigations have been mixed, with 2 prominent studies showing negative findings for efficacy. In the PROXI trial, a large Danish randomized controlled trial studied 1400 patients undergoing abdominal surgery, who received either 80% oxygen or 30% oxygen during and for 2 hours after surgery. There was no significant difference in SSI rates with increased perioperative oxygen fraction. In addition, subsequent subgroup analysis of the PROXI study showed there was increased long-term mortality in the high inspired oxygen group, with patients undergoing cancer surgery, although this secondary finding of mortality difference is controversial because of potential confounding, sample size, and lack of a convincing biological mechanism.

Several conducted meta-analyses of these trials do suggest an overall reduction of SSI rates. There is significant heterogeneity of the trials performed, with variability of the type of surgical procedures, perioperative care, and delivery protocol for hyperoxia. Perioperative hyperoxia has been included in some recommendations for the prevention of SSIs.

Perioperative measures with considerably less controversy include perioperative warming, hair removal, and optimization of the operating room environment. Perioperative hypothermia is associated with significantly increased risk of SSI. With regards to hair removal, the lowest risk of SSI has always been associated with not removing hair. If hair needs to be removed because of interference with the procedure, then hair removal should be done immediately before the surgery with a clipper rather a razor.

The development of further preventative measures will require additional research, combining both basic and clinical research. Even with the existing measures, there continue to be areas that are controversial due to the conflicting data available. As baseline SSI rates decline with improving standard of care, identification of additional methods of prevention will continue to become more challenging.

MAJOR LIMITATIONS IN PREVENTION

In an ideal scenario, primary prevention is completely effective and the burden of SSI-related morbidity is reduced to 0%. As described in later discussion, the relationship between compliance with evidence-based guidelines and SSI outcomes is imperfect. With the risk inherent with nonmodifiable risk factors, there will likely be a minimum prevalence that cannot be entirely eliminated. In addition, with the development of numerous evidence-based guidelines, there continue to be hurdles with implementation and translation of these guidelines to practice.

In several jurisdictions, there is incomplete compliance with guidelines, even when associated with checklists, pathways, and packages. Compliance itself is a multifactorial issue that can be limited by a host of factors. Compliance can be limited by lack of awareness of guidelines by members of the multidisciplinary health care team. Lack of awareness of specific guidelines can occur even though SSI outcomes are considered to be important and major determinants of health care outcomes. Local regional campaigns to improve compliance with these measures are also resource-intensive and can be associated with marginal improvement in both compliance and outcomes.

THERAPY

The general principle of SSI therapy remains control of the source of infection. For superficial SSI, the standard management remains the use of incision and
The wound should be sufficiently sized to promote adequate drainage. A variety of local wound care options are available, with the simplest being saline-soaked cotton gauze dressings. For uncomplicated superficial SSIs, simple incision and drainage, with local wound care, are appropriate, with no antibiotic therapy required.

Identification of deep SSI or complicated skin and soft tissue infection requires adequate clinical suspicion. The presence of systemic features (eg, fever or leukocytosis) with an absence of local signs of wound infection should raise suspicion for organ/space SSI, or for an infection arising from an alternate site. In addition, consideration should be made for antibiotic therapy in SSIs in patients with systemic features, or widening erythema (>5 cm in diameter). Direct clinical examination should follow to ensure an appropriate clinical response, with consideration of alternative diagnoses, if atypical features were to appear.

For more complicated skin and soft tissue infections, antibiotic therapy is appropriate, particularly in patients demonstrating signs of systemic shock. The principle of source control remains important, with the appropriate selection of antibiotics based on the type of surgical procedure performed, and the expected microbial causes for the infection. As highlighted earlier, the growing impact of MDR organisms will greatly increase the difficulty of treatment of SSIs. Effective prevention will help to limit the potential impact of increasing resistance.

THE ECONOMIC AND QUALITY OF CARE IMPACT OF SURGICAL SITE INFECTIONS

The economic costs of SSIs are significant because of the volumes of cases that are seen, with an annual 2.7 million operative procedures performed in the United States. Even with a conservative estimate of more than 290,000 cases of SSI, there is a substantial economic cost to the management of SSI. There is a wide variance in estimates of the attributable costs of SSI infection that depends heavily on the type of surgical procedure and the geographic region studied. There is additional confounding of the economic cost estimates due the lack of risk stratification of patient populations studied, and methods of cost summation. The estimates vary from $3937 per infection (Canadian tertiary care hospital) to about $20,000 per infection (American orthopedic surgery population). These analyses may underestimate the economic impact, through a combination of underestimation of surgical infection rates, and the costs of the worst manifestations of SSI, such as organ/space SSI with accompanying sepsis and septic shock, which can exceed $22,100 per case.

The rates of SSI are increasingly being used as outcome and surrogate measures for examining the quality of surgical care. The National Surgical Infection Prevention Project was developed in 2003 with the goal to standardize quality improvement measures to decrease the incidence of SSI in major surgical procedures nationally. This project has now transitioned to the Surgical Care Improvement Project (SCIP) in 2005, which included the SSI measures (Table 4) and additional performance measures of cardiac, respiratory, and thromboembolic complications.

In some countries these quality indicators have become pay-performance measures. For example, in the United States, the Centers for Medicare and Medicaid Services linked Medicare payments to hospitals on their compliance to performance indicators. The 2014 hospital payment rule finalized the general framework for the Hospital-Acquired Condition Reduction Program to be implemented in 2015. The rule updated measures and financial incentives with the following areas related to SSI: postoperative sepsis rate, wound dehiscence rate, central line–associated bloodstream infection, and catheter-associated urinary tract infection. The 2 new
measures added of health care–associated infections were hospital-onset MRSA bacteremia and *Clostridium difficile*.103

There have been conflicting results with studies examining the compliance of the SCIP and the effect on SSI rates. Some studies have shown significantly lower SSI rates in hospital groups with higher compliance rates with 2 specific SCIP measures (appropriate antibiotic timing and antibiotic selection).104 Another study showed if at least 2 of the 7 (see Table 3) measures were done there was a significant decrease in the SSI rate; however, compliance of just one of the SCIP did not result in benefit.105 Although other studies have shown that adherence to multiple SCIP measures did not correlate with a decrease of SSI,106,107 these studies demonstrate it is more than just compliance to specific metric that influences outcome in SSI. The emphasis cannot be only on adherence reporting but instead focused on a culture of safety and quality within the team.

**SUMMARY**

SSIs remain a very important component of patient outcome, contributing to substantial patient morbidity. From a historical perspective, there has been a significant improvement in postsurgical outcomes, but these incremental gains have slowed in the recent decades. The translation of basic and clinical research has expanded the complexity of evidence-based guidelines for SSI prevention. The importance of SSI prevention has been heightened because of its association with institutional and regulatory quality control measures. Sustained research in multiple aspects of SSI prevention needs to continue to realize further gains in SSI prevention. A multidisciplinary and multifaceted approach to SSI is absolutely necessary to continue to improve these critical outcomes of surgery.

**REFERENCES**


