Prevention of Perioperative Infection

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Current Concepts Review

Prevention of Perioperative Infection

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- Administration of preoperative antibiotics is associated with reduced rates of surgical site infections.
- Antibiotics should be continued for no longer than twenty-four hours after elective surgery or surgical treatment of closed fractures.
- Chlorhexidine gluconate is superior to povidone-iodine for preoperative antisepsis for the patient and surgeon.
- Closed suction drainage is not warranted in elective total joint replacement. It is associated with an increased relative risk of transfusions. Drains left in situ for more than twenty-four hours are at an increased risk for bacterial contamination.
- The rate of postoperative infections associated with occlusive dressings is lower than that associated with nonocclusive dressings.
- Appropriate management of blood glucose levels, oxygenation, and the temperature of the patient reduces the risk of postoperative infection.

Surgical site infection is one of the most common complications that a surgeon encounters, with an infection occurring after approximately 780,000 operations in the United States each year[1]. In the era of evidence-based medicine, it is in the best interest of patients and physicians to follow practices backed by basic science and clinical data. Unfortunately, standards of practice, even for the use of prophylactic antibiotics, are frequently not followed[2]. In 2005, this journal made a commitment to present physicians with the literature to support the best available treatment for their patients with use of "recommendations for care" based on grades of recommendation in review articles[3]. Grades of recommendation are intended to guide surgeons in determining whether they should change their practice on the basis of good (Grade-A) or fair (Grade-B) recommendations. Grade-A recommendations are generated from Level-I studies, whereas Grade-B recommendations are derived from Level-II or III research. A proposal is considered to be Grade C when there is poor or conflicting evidence concerning an intervention based on Level-IV or V studies, and Grade I indicates that evidence is inadequate to make a recommendation[4]. We have provided these recommendations in this article, and we have also provided a level-of-evidence grade for individual studies. Methods for determining levels of evidence were introduced in this journal in 2003 and have been shown to be reliable and reproducible[5,6].

The current article synthesizes the best available evidence regarding use of preoperative antibiotics before elective and emergent orthopaedic operations, preoperative skin preparation of the patient and surgeon, operating-room issues, wound closure, operative drainage, and use of dressings in the hope that it will help physicians to reduce the incidence of postoperative wound infection. The management and effect of important patient factors such as smoking, nutritional status, immunocompromise, medications, cardiovascular status, obesity, and other major comorbidities will not be addressed here. The reader is instead referred to an excellent review of these topics by Gurkan and Wenz[7].

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Antibiotic Issues

Proven Benefits of Antimicrobial Prophylaxis

The use of antibiotic prophylaxis in orthopaedic surgery has been shown to be beneficial. Initially, there was some debate about whether antibiotics administered prior to surgery would be of any benefit or worth the risk[8]. Multiple prospective, double-blind studies support the use of antibiotic prophylaxis in the settings of closed fractures and total joint arthroplasty[9-16] (see Appendix).

The benefits of antibiotic prophylaxis have been substantiated in studies of open fractures, for which antibiotics have been shown to be effective as long as they target the usual infecting organisms[17]. In a prospective randomized trial, Patzakis and Wilkins found that the preoperative administration of appropriate antibiotics was the most important factor in determining the rate of wound infection in association with open fractures[18]. The Cochrane Database of Systematic Reviews also endorses the practice of treating open fractures with prophylactic antibiotics[19].

Choice of Antibiotic

Bacterial contamination and eventual infection most often come from skin or airborne sources[20,21]. The most common organisms that cause deep wound infection are *Staphylococcus aureus* and coagulase-negative staphylococci such as *Staphylococcus epidermidis*[20,22-24]. Therefore either cefazolin or cefuroxime should be used in conjunction with hip or knee arthroplasty, fixation of closed fractures, and most elective orthopaedic procedures[2,22,25-27].

Systemic antibiotic prophylaxis for patients with an open fracture has recently been systematically reviewed by the Surgical Infection Society (SIS)[28] and the Eastern Association for the Surgery of Trauma (EAST)[29]. Each group developed recommendations on the basis of the classic classification system described by Gustilo and Anderson in 1976 and the subsequent modification by Gustilo et al. in 1984 (see Appendix)[30-32]. Both analyses[28,29] provided substantial evidence that antibiotic prophylaxis for type-I open fractures should include a first-generation cephalosporin. Traditional teaching has asserted that coverage against gram-negative organisms is required for all type-III and perhaps some type-II fractures because of the increased contamination and higher-energy mechanism associated with these fractures. A penicillin has also been added to the prophylactic regimen for fractures at risk for clostridial contamination[33]. The SIS and EAST groups differ with regard to their support of these principles. The EAST group recommends the use of additional coverage against gram-negative organisms on the basis of evidence that “gram negative organisms are cultured from type III wounds after initial débridement.”[29] This statement is somewhat misleading as, to our knowledge, no recent investigations have shown any relationship between the results of cultures performed at the time of the initial presentation and the causative bacteria grown on culture during the management of a subsequent infection[34-36]. The SIS group, citing the bacterial resistance patterns reported by Patzakis et al.[17] in their seminal study in 1974, failed to find any outcomes data to support coverage against gram-negative bacteria. While two studies have shown that administration of gentamicin once daily is effective prophylaxis for patients with a type-II or III open fracture[37,38], this regimen has not been compared with other antibiotic regimens, to our knowledge. The SIS group also suggested that penicillin G may not be the optimal therapy for clostridial infections, citing several studies of animals by Stevens et al.[39-41], although the EAST group still recommends prophylaxis with penicillin for patients with a fracture at risk for clostridial contamination. A Grade-A recommendation can be made for the administration of a type-I cephalosporin for all open fractures. Despite their widespread use, there is currently insufficient evidence to support the use of aminoglycosides in the management of type-II and III open fractures. There is also not enough data to make recommendations (Grade I) regarding the use of penicillin for contaminated open fractures. This area clearly needs to be explored further in randomized controlled studies.

Vancomycin or clindamycin may be used for patients with an allergy or adverse reaction to beta-lactam antibiotics. To our knowledge, no one has compared the efficacy of clindamycin with that of vancomycin for prophylaxis against infection, and thus no recommendation can be made (Grade I) regarding the use of one antibiotic over the other for patients with an allergy to beta-lactam agents. Cross reactivity between cephalosporins and penicillins has historically been reported to be >10%; however, this percentage has been questioned in the recent literature because of the lack of confirmation of the allergy with skin-testing. Current data suggest a much lower risk of cross reactivity[42]. Anaphylaxis to cephalosporin is exceedingly rare, with the rate ranging from 0.0001% to 0.1%[43]. Li et al. assessed sixty patients with a documented allergy to penicillin or cephalosporin who were evaluated preoperatively by an allergist[44]. Fifty-nine of these patients were given a penicillin-allergy skin test, and 93% (fifty-five) of the fifty-nine had a negative result of that test. Ninety percent (fifty-four) of the sixty patients in the series were cleared by the allergist to receive a cephalosporin. No patient had an allergic reaction. Nonetheless, multiple studies have shown a four to tenfold risk of cross reactivity in patients with a documented allergy to penicillin who are subsequently given a cephalosporin, and more than one expert panel has recommended the use of vancomycin for such patients[28,45].

Timing of Antibiotic Administration

Antibiotics should be administered within sixty minutes prior to the incision[46,47] and, ideally, as near to the time of the incision as possible[48-50]. An additional intraoperative dose is advised if the duration of the procedure exceeds one to two times the half-life of the antibiotic or if there is substantial blood loss during the procedure[51]. The American Academy of Orthopaedic Surgeons has developed recommendations regarding the frequency of intraoperative antibiotic administration (Table I)[52]. One potential method of ensuring preoperative, and if necessary subsequent intraoperative, administration of antibiotics in hospitals in which anesthesiologists track patients electronically is to include a computerized alert that reminds anesthetists and surgeons to provide the appropriate antibiotics[53].

Vancomycin Usage

Vancomycin may be used for patients with known colonization with methicillin-resistant *Staphylococcus aureus* or in facilities with recent outbreaks of methicillin-resistant *Staphylococcus aureus* infections. Vancomycin may also be used for patients who have hypersensitivity to penicillin. Excessive use of vancomycin promotes the formation of resistant organisms[54-59]. Vancomycin should be started within two hours prior to the incision because of its extended infusion time. The infusion time is extended to prevent the adverse reactions that are sometimes associated with vancomycin infusion, such as hypotension or chest pain mimicking myocardial infarction[60]. H1 and H2 histamine receptor blockers allow more rapid infusion[61,62].

Two randomized trials failed to demonstrate a benefit of vancomycin compared with cefazolin[63] or cefuroxime[64] for preventing perioperative infections, although there was a lower prevalence of methicillin-resistant *Staphylococcus aureus* infections in patients treated with vancomycin. Vancomycin may be warranted for certain procedures in institutions where methicillin-resistant *Staphylococcus aureus* infection is an important problem or if the patient has identifiable risk factors, such as recent hospitalization, renal disease, or diabetes[2].

Duration of Antibiotic Administration

Current data support minimizing the duration of antibiotic administration. The postoperative duration of routine antibiotic use has decreased from multiple days to twenty-four hours. Some surgeons prefer a single dose. Research by Nelson et al. supports prophylactic antibiotic administration for twenty-four hours after total hip or total knee arthroplasty or hip fracture surgery[65]. In their randomized controlled trial, 358 patients received prophylactic nafcillin or cefazolin for twenty-four hours or seven days. There was no significant difference in the prevalence of surgical site infection between the groups at six weeks or one year. Williams and Gustilo retrospectively compared the outcomes for 1341 patients who had received prophylaxis for three days following total joint arthroplasty with those for 450 patients who had received it for one day[66]. An infection developed in eight (0.6%) of the 1341 patients in the first group compared with three (0.67%) of the 450 in the second group. Pollard et al.[67] and Mauerhan et al.[23] also found that the infection risk following twenty-four hours of antibiotic administration was no higher than that following three or fourteen days of administration.

A single dose of antibiotics may be adequate for prophylaxis against perioperative infection. A randomized controlled trial of 466 patients treated with total joint arthroplasty showed no significant difference in the rate of surgical site infection between the group that had received a single dose of antibiotics and groups that had received prophylaxis for two, three, or seven days[68]. The authors noted that the use of single-dose prophylaxis instead of forty-eight hours of prophylaxis would save $7.7 million per 100,000 patients. Using antibiotics for two days postoperatively instead of for seven days postoperatively would save $29.7 million per 100,000 patients. In a larger randomized controlled trial of 1489 patients with a closed fracture, Garcia et al. also demonstrated results that favor the use of a single prophylactic dose[69]. The difference in the infection rate among treatment groups receiving one dose of cefonicid, three doses of cefamandole, or five doses of cefamandole was not significant.

The proper duration of antibiotic prophylaxis for open fractures is not well established. Perhaps the lack of consensus about the treatment protocol is due to the high variability among open fractures and the poor interobserver reliability of the classifications of these injuries. On the basis of their extensive reviews, the SIS and EAST groups both recommended the use of prophylactic antibiotics for twenty-four hours postoperatively for patients with a type-I open fracture and for forty-eight to seventy-two hours for those with a type-III open fracture. The two groups differ with regard to their recommendations about the duration of antibiotic use for patients with a type-II fracture. EAST advocates twenty-four hours of prophylaxis, and SIS recommends forty-eight hours. The lack of data supporting longer antibiotic prophylaxis suggests that administration for forty-eight hours following débridement of open fractures is not clinically warranted. Two prospective Level-I studies failed to show a difference in infection rates between a single dose of antibiotics and intravenous administration of antibiotics for five days in patients treated for an open fracture[70,71]. Multiple studies have shown that extending antibiotic prophylaxis may actually increase the risk of resistant pneumonia and other systemic bacterial infections[72-76].

Local Antibiotics

Antibiotics may also be delivered locally, with use of impregnated cement beads, spacers, or premolded implants. Local antibiotic delivery requires a delivery vehicle, most commonly polymethylmethacrylate cement, and an antimicrobial agent available in a powder form. Two to 4 g of tobramycin and 2 g of vancomycin per 70-g bag of cement are often used because they are active against the most common microbes and are heat-stable. Systemic toxicity is not a concern[77]. The eluted antibiotic represents a small percentage of the total amount of antibiotic present, and elution mainly occurs dur-

TABLE I Recommendations by the American Academy of Orthopaedic Surgeons for Repeat Doses of Antibiotics[52]

Antibiotic	Frequency of Administration
Cefazolin	Every 2-5 hours
Cefuroxime	Every 3-4 hours
Clindamycin	Every 3-6 hours
Vancomycin	Every 6-12 hours

TABLE II Recommendations for Perioperative Administration of Antibiotics[3]

Grade of Recommendation	Recommendations
A	Broad-spectrum antibiotics should be administered within one hour of incision time and may be continued up to twenty-four hours postoperatively. Longer antibiotic prophylaxis is not warranted in elective procedures or closed fracture care Patients with an open fracture should receive antibiotics urgently, and administration should be continued for twenty-four hours postoperatively. A first-generation cephalosporin should be used for all open fractures when not otherwise contraindicated
B	Vancomycin appears to be equivalent to a first-generation cephalosporin in the prevention of perioperative infection when there is no history of methicillin-resistant *Staphylococcus aureus* infection
C	Local antibiotics may help reduce the rate of infection and osteomyelitis in association with open fractures Vancomycin may be used as antibiotic prophylaxis in patients with a beta-lactam allergy
I	Aminoglycosides may decrease the prevalence of infection in association with Gustilo and Anderson type-II and III open fractures There is inadequate evidence to support the use of penicillin to prevent clostridial infection in patients with a severely contaminated open fracture There is inadequate evidence to suggest that either clindamycin or vancomycin is superior to the other for antibiotic prophylaxis in patients with beta-lactam allergy

ing the first twenty-four hours[78,79]. For a more comprehensive analysis of the basic science and clinical benefits of local antibiotics in patients undergoing high-risk joint reconstruction, the reader is referred to the excellent review by Jiranek et al.[80].

To our knowledge, no major prospective randomized control trials have shown a benefit to the use of local antibiotics compared with intravenous systemic antibiotics, but multiple retrospective series have suggested benefits of local antibiotics. Henry et al. found that the use of an antibiotic bead pouch decreased the prevalence of wound infection and osteomyelitis associated with open fractures; however, this increase was in comparison with the rate in historical controls[81]. Keating et al. examined the benefit of the antibiotic-bead-pouch technique in a study of eighty-one open tibial fractures treated with intramedullary stabilization and either systemic antibiotics alone (twenty-six fractures) or a combination of systemic antibiotics and local tobramycin beads (fifty-five fractures)[82]. They found fewer deep infections in the patients managed with the combination of systemic and local antibiotics; however, this result was not significant ($p = 0.12$). Ostermann et al. performed a retrospective review of 1085 open fractures treated with either systemic antibiotics alone (240 fractures) or systemic and local antibiotics (845 fractures)[83]. The infection rate was significantly reduced by the use of local and systemic antibiotics (infection rate, 3.7% [thirty-one of 845]) rather than systemic antibiotics alone (infection rate, 12% [twenty-nine of 240]; $p < 0.001$). The reduction in the rate of acute osteomyelitis was significant in the patients with a type-IIIB or IIIC fracture, and the reduction in the rate of chronic osteomyelitis was significant in those with a type-II or IIIB fracture[83]. This study has been criticized because a disproportionate number of wounds were left open in the group treated with systemic antibiotics, compared with the group treated with the bead pouch, potentially increasing the risk of local wound infection[84]. We are aware of only one randomized trial involving use of the antibiotic bead pouch[85]. This study, in which open fractures were managed with either systemic antibiotics or local antibiotics after a single preoperative prophylactic dose had been given in the emergency department, did not demonstrate a benefit in association with local administration ($p > 0.05$). The study was underpowered, and the follow-up rate was only 60%.

In summary, preoperative antibiotics have become the standard of care before the vast majority of orthopaedic procedures (Table II). The decision regarding whether to administer an additional dose of antibiotics intraoperatively should be based on the half-life of the particular antibiotic. Vancomycin or clindamycin should be given to patients with a documented allergy to penicillin. Antibiotic use should be stopped as soon as possible after the surgery; however, there is still controversy regarding the appropriate duration of antibiotic coverage in association with both elective procedures and procedures for traumatic injuries. Anecdotal clinical and basic-science[86] evidence supports the use of local antibiotics for patients with an open fracture; however, a large prospective randomized trial is needed to better delineate the clinical role of antibiotic-impregnated beads in this subset of skeletal injuries.

Preoperative Hair Removal

Preoperative shaving of the surgical site is common practice, but there is a scarcity of data to support its use. Several authors have denounced shaving on the night before the operation because of an increased risk of surgical site infection as a result of many microscopic cuts in the epidermis, which

TABLE III Recommendations for Patient Preparation and Surgical Scrubs

Grade of Recommendation	Recommendations
A	Compared with povidone-iodine, chlorhexidine surgical scrub provides a prolonged reduction in skin contamination with less toxicity and skin irritation
	Aqueous surgical hand-rubs are equivalent to traditional surgical scrubs with regard to their ability to reduce bacterial contamination. Surgeons comply with hand-rub protocols better than they comply with surgical scrub protocols
	A patient's temperature, oxygenation, and serum blood glucose level should be optimized in the perioperative period
B	The use of iodophor-impregnated surgical drapes decreases skin contamination but does not appear to reduce infection rates
	The use of laminar flow in the operating room is associated with decreased rates of wound infections and wound contamination
	Hair removal preoperatively should be minimized and, if necessary, performed with clippers or depilatory products

harbor bacteria[87]. Clippers do not come into contact with the skin itself and have been associated with a reduction in postoperative infection rates[88-90]. A meta-analysis by the Cochrane group showed that the relative risk of a surgical site infection following hair removal with a razor was significantly higher than that following hair removal with clippers (relative risk, 2.02; 95% confidence interval, 1.21 to 3.36)[91]. Furthermore, the analysis showed no difference in the rate of postoperative infections between procedures preceded by hair removal and those performed without hair removal. Whenever hair is removed, clippers, rather than a razor, should be used at the time of surgery (Table III)[92].

Preoperative Skin Antisepsis

Patients

The most commonly used antiseptic agents for surgical scrubbing include chlorhexidine gluconate, alcohol-based solutions, and iodophors such as povidone-iodine. Chlorhexidine gluconate acts to disrupt the cellular membranes of bacteria and is favored for its long-lasting activity against gram-positive and gram-negative organisms found on human skin. The iodophors also act against common skin flora; however, their activity is much shorter than that of chlorhexidine gluconate. Chlorhexidine gluconate and povidone-iodine both reduce bacterial counts on contact; however, this effect is sustained longer in skin cleaned with chlorhexidine. Furthermore, unlike chlorhexidine gluconate, the iodophors can be inactivated by blood or serum proteins and should be allowed to dry in order to maximize their antimicrobial action[93]. Alcohol is an excellent antimicrobial and has germicidal activity against bacteria, fungi, and viruses. The effectiveness of pure alcohol solutions is limited by their lack of any residual activity and their flammability (see Appendix). A recent meta-analysis showed no difference in efficacy among skin antiseptics used in clean surgery; however, the rarity of infection in such situations probably explains the low power of the included studies[94].

Foot and ankle surgery is often complicated by infection due to local contamination[95,96]. Infection rates associated with ankle arthrodesis have been as high as 19%[97], whereas fusion of the subtalar joint is followed by an infection approximately 6% of the time[95,98]. Between 36% and 80% of cultures of specimens taken from the forefoot after preparation with a povidone-iodine scrub and paint are positive compared with 0% to 28% of cultures of specimens taken from the anterior aspect of the ankle after such preparation[99,100]. Ostrander et al. found fewer bacteria on feet prepared with ChloraPrep (2% chlorhexidine gluconate and 70% isopropyl alcohol; Medi-Flex, Overland Park, Kansas) than on those prepared with DuraPrep (0.7% iodin and 74% isopropyl alcohol; 3M Healthcare, St. Paul, Minnesota) or Techni-Care (3.0% chloroxylenol; Care-Tech Laboratories, St. Louis, Missouri)[101]. There was no difference in infection rates among the three groups. Keblish et al. quantitatively assessed skin contamination on feet cleaned with one of four methods: a povidone-iodine paint and scrub, a povidone-iodine paint and scrub after an isopropyl alcohol scrub, povidone-iodine scrub brushing, and isopropyl alcohol scrub brushing[100]. There were significantly fewer positive cultures of specimens from hallucal folds of the feet prepared with the isopropyl alcohol scrub brushing (12% compared with 76% for the group prepared with povidone-iodine scrub brushing, $p < 0.001$). The use of a brush to apply the cleansing agent was also superior to the use of a standard applicator in reducing the number of positive cultures of specimens from web spaces.

In vitro studies have provided strong evidence that povidone-iodine may impair wound-healing. Cooper et al. evaluated the toxicity of common wound irrigants with use of a proven cell-viability assay and found povidone-iodine, even in concentrations of 0.5% (1/20th) of those used in clinical practice, to be extremely toxic to fibroblasts and keratinocytes[102]. Thus, povidone-iodine should not be used for preparation of open wounds or on postoperative dressings[103].

The current literature strongly suggests that chlorhexidine gluconate is superior to povidone-iodine for preoperative antisepsis for patients (Table III). Alcohol is an excellent antimicrobial, but its benefit is limited by its lack of residual activity. Use of a combination of chlorhexidine gluconate and alcohol is perhaps a way to take advantage of their antiseptic properties.

Surgeon

The current choices of antiseptic for the surgeon scrub mimic those used for the patient scrub. Aly and Maibach compared the antibacterial efficacy of a two-minute scrub with chlorhexidine gluconate with the efficacy of a two-minute scrub with povidone-iodine at three time-points: immediately after scrubbing, three hours later, and six hours later[93]. Chlorhexidine gluconate achieved significantly ($p < 0.01$) greater adjusted mean log bacterial count reductions than did povidone-iodine at all sampling times.

Parienti et al. compared the effectiveness of aqueous alcohol hand-rubs with that of traditional povidone-iodine or chlorhexidine gluconate scrubbing with a scrub brush before 4387 clean or clean-contaminated operations[104]. There was no difference in wound infection rates (2.44% for the alcohol group compared with 2.48% for the povidone-iodine or chlorhexidine gluconate group), but physician compliance with the alcohol protocol was better than that with the other protocol (44% compared with 28%; $p = 0.008$), and there were fewer complaints about skin dryness and irritation. These clinical findings were substantiated by Bryce et al.[105]. Larson et al. also compared an alcohol rub with an antiseptic scrub in their study of twenty-five physicians[106]. Beginning on day 5 of the study, the bacterial counts yielded by the scrubless preparation (containing 61% ethyl alcohol, 1% chlorhexidine gluconate, and emollients) were found to be significantly decreased compared with those yielded by the traditional scrub containing 4% chlorhexidine gluconate. The alcohol rub also decreased skin damage ($p = 0.002$) and required less time ($p < 0.0001$) than the traditional chlorhexidine gluconate scrub. Pereira et al. also showed that prolonged use of alcohol and chlorhexidine gluconate rubs had better antibacterial efficacy than both traditional povidone-iodine and traditional chlorhexidine gluconate scrubbing regimens[107].

Grabsch et al. compared the traditional povidone-iodine scrub with a regimen that involved a traditional chlorhexidine gluconate scrub plus a chlorhexidine gluconate-alcohol rub[108]. The authors reported that bacterial counts immediately after scrubbing were reduced to a greater extent in the chlorhexidine gluconate treatment arm than in the povidone-iodine treatment arm ($p < 0.001$), a finding most likely due to the additional rapid action of alcohol in the chlorhexidine gluconate protocol. A persistent and cumulative antimicrobial effect was also found with a repeated chlorhexidine gluconate-alcohol rub prior to any additional operations ($p < 0.001$). A cross-over trial conducted by Nishimura directly compared povidone iodine-ethanol and chlorhexidine gluconate-ethanol brushless scrubs after an initial povidone-iodine brushless scrub[109]. The reduction in the bacterial count in the povidone iodine-ethanol group was significantly higher than that in the chlorhexidine gluconate-ethanol group immediately after washing ($p < 0.001$), but it was roughly equivalent two hours later. This finding illustrates the more rapid antiseptic effects of povidone-iodine and/or the longer-lasting effects of chlorhexidine gluconate. Most data indicate that povidone-iodine and chlorhexidine gluconate have equal efficacy in decreasing the initial bacterial contamination of the skin of a patient or surgeon, but chlorhexidine gluconate has a longer effect, is less toxic in open wounds, and causes less skin irritation with prolonged use (see Appendix)[106-108].

Chlorhexidine gluconate-based surgical scrubs decrease skin colony counts. Traditional scrub brushes or combination aqueous alcohol rubs are equally efficacious. Physicians' compliance with the use of aqueous rubs may be better than their compliance with regimens requiring the use of scrub brushes (Table III).

Occlusive Drapes

Ioban iodophor-impregnated plastic drapes (3M Health Care) have been shown in the critical care and obstetrical literature to reduce postoperative wound contamination as measured by positive cultures of specimens obtained from the skin[110,111]. The orthopaedic literature pertaining to iodophor-impregnated drapes has shown a reduction in wound contamination without any concurrent decrease in wound infection. Ritter and Campbell found no difference in wound infection rates following 649 total joint replacements for which preparation was performed with either an iodine spray or a combination of alcohol and an Ioban drape[112]. In a recent randomized controlled trial, Jacobson et al. evaluated the use of an Ioban drape in conjunction with either 3M DuraPrep Surgical Solution or povidone-iodine scrub and found no significant difference in wound contamination between the two groups[113]. The use of impregnated plastic drapes does not appear to reduce the prevalence of infection (Table III).

Irrigation

Wound irrigation removes debris, foreign material, and blood clots while decreasing bacterial contamination. Several in vitro and in vivo studies have shown that high-pressure pulsatile lavage is more effective than low-pressure pulsatile lavage for removing particulate matter, bacteria, and necrotic tissue. This effect is more pronounced in contaminated wounds treated in a delayed manner[114-117]. There is substantial concern, however, that high-pressure pulsatile lavage and low-pressure pulsatile lavage result in higher rates of deep bacterial seeding in bone than does brush and bulb-syringe lavage and that higher irrigant pressures result in greater osseous damage and perhaps impairment of osseous healing. Kalteis et al. showed that high-pressure pulsatile lavage was superior to low-pressure pulsatile lavage and manual rinsing and was as effective as brush cleaning in removing *Escherichia coli* from human femoral heads in vitro[118]. The study also revealed that, compared with brush and bulb-syringe lavage, high and low-pressure pulsatile lavage resulted in significantly ($p < 0.001$) higher rates of deep bacterial seeding in bone. Using an in vitro contaminated human tibial fracture model, Bhandari et al. also showed that high-pressure pulsatile lavage results in bacterial seeding of the medullary canal[119]. High-pressure pulsatile lavage successfully removed almost 99% of the bacterial burden at the fracture surface; however, there was a higher number of positive bacterial cultures of specimens obtained between 1 and 4 cm from the fracture site than there were in nonirrigated controls ($p < 0.01$).

Similar bacterial seeding may be seen in muscle tissue after pulsatile irrigation. Hassinger et al. showed that ovine muscle samples subjected to high-pressure pulsatile lavage had a significantly greater depth of bacterial penetration and greater numbers of colonizing bacteria when compared with samples subjected to low-pressure pulsatile lavage ($p < 0.05$)[120]. Bhandari et al. found that both high and low-pressure pulsatile lavage removed bacteria for up to three hours after the initial contamination; however, high-pressure pulsatile lavage was more effective after this time ($p < 0.05$)[121]. High-pressure pulsatile lavage was also shown to increase muscle damage and decrease particulate removal when it was compared with bulb-suction irrigation in vitro[122].

Recent studies have suggested that high-pressure pulsatile lavage may also damage the architecture of cancellous bone. Dirschl et al. found that high-pressure irrigation of osteotomized rabbit femora decreased the amount of new bone formation during the first week following a distal femoral osteotomy compared with that seen after bulb-syringe irrigation[123]. This difference became negligible during the second week after the osteotomy. In a rat model, high-pressure pulsatile lavage decreased the mechanical strength of a fracture callus during the first three weeks of fracture-healing compared with that observed following bulb-syringe irrigation ($p < 0.05$)[124].

Previous reviews have suggested that high-pressure pulsatile lavage should perhaps be reserved for severely contaminated wounds or for open injuries for which treatment will be delayed. Low-pressure irrigation should be used if contamination is minimal or treatment is immediate. Although Anglen suggested the use of 3 L of irrigation fluid for type-I open fractures, 6 L for type-II, and 9 L for type-III[125], these recommendations have not been supported by clinical data.

Recent studies comparing the efficacy of antibiotic solutions with that of detergent irrigants have made a strong case for the incorporation of detergents in wound irrigation. Detergents such as castile soap or benzalkonium chloride are effective in decreasing the burden of bacteria in musculoskeletal wounds because of their surface-active properties. The detergents act by disrupting hydrophobic and electrostatic forces, thereby inhibiting the ability of bacteria to bind to soft tissue and bone. In an in vitro study by Anglen et al., castile soap was superior to antibiotic-containing irrigants and normal saline solution when it came to removing bacteria from steel, titanium, muscle, and bone[126]. In vivo rat studies have shown that castile soap is very effective in preventing *Pseudomonas aeruginosa* infection, and benzalkonium chloride was most effective against *Staphylococcus aureus*[127]. Wounds irrigated with benzalkonium chloride alone have a higher risk of dehiscence and breakdown. This led to the development of a sequential irrigation protocol involving castile soap, saline solution, benzalkonium chloride, and a final saline solution rinse, which was more effective than saline solution irrigation without the complications of wound breakdown seen with benzalkonium chloride alone[128]. Anglen conducted a prospective, randomized study of 458 lower-extremity open fractures in which he compared castile soap irrigation with bacitracin irrigation[129]. There was no significant difference between groups with respect to the rate of surgical site infection or bone-healing de-

TABLE IV Recommendations Regarding Surgical Drains and Wound Management

Grade of Recommendation	Recommendations
A	Use of surgical drains in joint replacement surgery or closed fracture care is associated with more blood transfusions but not with any increase in the rate of hematomas, wound infections, reoperations, or thromboembolic disease or in the hospital stay, when compared with operations performed without a drain
	The rate of surgical site infection associated with occlusive dressings is lower than that associated with nonocclusive dressings
B	Surgical dressings may be removed as early as the first postoperative day without any apparent increase in the risk of infection
	Triple antibiotic ointment increases epithelialization and has been associated with fewer infections in uncomplicated clean surgical wounds
I	High-pressure pulsatile lavage removed more debris than did low-pressure pulsatile or bulb-syringe lavage in an animal model, although the higher pressure may cause damage to bone and muscle
	Castile soap irrigation appears to remove more bacteria than bacitracin does and may be associated with fewer wound-healing problems in an animal model
	There is no apparent difference among wound closure techniques with regard to the rate of wound infections
	There is insufficient evidence to support or refute the benefits of closure of dead space in patients undergoing orthopaedic surgery

lay, but the fractures irrigated with bacitracin were associated with a significantly higher rate of wound-healing problems (9.5%, nineteen of 199 fractures) than were those irrigated with castile soap (4%, eight of 199 fractures; $p = 0.03$).

Irrigation of wounds and, in particular, open fractures plays an important role in the reduction of infection (Table IV). Use of a low-to-intermediate pressure setting minimizes bone and soft-tissue damage while allowing removal of bacteria and particulate matter. Irrigation with castile soap improves organic removal and may be associated with fewer problems with wound-healing when compared with irrigation with antibiotic solution.

Postoperative Drains

Drains have traditionally been used in an attempt to decrease the formation of a postoperative hematoma and manage dead space while providing a conduit for the egress of material from the wound. Studies of animals have shown more retrograde bacterial migration with the use of simple conduit drains than with the use of closed suction drains[130]. Sorensen and Sorensen evaluated 489 clean orthopaedic procedures, including those performed for hip fractures and hip and knee arthroplasties, in a prospective cohort study[131]. Fifty-six drain tips (11%) were found to be contaminated as evidenced by a positive culture; however, only five patients (1%) were infected by the same bacteria as had grown on culture of the tip specimen. Contaminated drain tips are associated with wound infections, whereas a negative tip-specimen culture is very rarely seen in the presence of wound infection[132]. Drinkwater and Neil placed drains in ninety-two patients undergoing hip or knee arthroplasty and removed them at randomly generated times during the first ninety-six hours postoperatively[133]. Only one contaminated drainage tip was found when the drain was removed in the first twenty-four hours postoperatively. Five (18%) of twenty-eight tips removed after twenty-four hours were found to be contaminated when a culture was performed, although the difference was not significant. In a retrospective analysis of more than 73,000 surgical patients with a wound infection, the presence of a surgical drain for more than twenty-four hours was associated with a higher likelihood that the wound would be infected with methicillin-resistant *Staphylococcus aureus* than with methicillin-sensitive *Staphylococcus aureus*[134].

The current orthopaedic literature has not shown an advantage to the use of drains in elective surgery. In a recent meta-analysis, Parker et al. evaluated the use of drains in 3689 joint-replacement surgical wounds[135]. The data showed no difference in rates of infection, wound hematomas, reoperations for wound complications, limb swelling, or thromboembolic complications and no difference in the hospital stay. Wound drainage was associated with a higher risk of transfusion (relative risk, 1.43). Two subsequent studies in the arthroplasty literature showed no benefit of the use of drainage in joint replacement[136,137].

The use of drains in fracture surgery has not been well evaluated. Two randomized controlled trials in which surgical drainage was compared with closure without a drain in clean orthopaedic procedures for traumatic injuries showed that drainage provided no benefit with respect to rates of infection, hematomas, transfusion, or revision surgery[138,139]. Two randomized studies also failed to show that the use of surgical drainage in elective lumbar spinal surgery reduced the rate of complications, including the formation of epidural hematomas or the development of a neurologic deficit[140,141]. In summary, Grade-A recommendations support the performance of operations without the use of a surgical drain. There is no evidence to suggest that use of a surgical drain prevents formation of a hematoma, infection, or wound dehiscence or influences other surgical outcomes (Table IV and Appendix).

Wound Closure

The literature on wound closure in orthopaedic procedures is sparse and primarily discusses its impact on the results of joint replacement surgery and arthroscopy portals. Comparative studies have involved subjective analysis of the appearance of the healed wound, inflammation, and patient satisfaction. The data are insufficient to make recommendations (Grade I) regarding appropriate wound-closure techniques (Table IV). The principle of maximizing blood flow while minimizing bacterial contamination and dead space has been studied. In a study in which laser Doppler flowmetry was used to evaluate cutaneous blood flow in association with various suture techniques, blood flow was significantly higher on the first postoperative day than it was on the fifth day and perfusion in wounds closed with subcutaneous sutures was greater than that in wounds closed with mattress sutures or surgical staples ($p = 0.048$)[142].

Contaminated wounds are associated with a higher risk of wound infection. Bacterial adherence to braided sutures is three to ten times higher than adherence to monofilament sutures[143,144]. Animal models have been used to evaluate closure of contaminated wounds[145]. Polglase and Nayman examined the use of subcuticular Dexon or transdermal sutures in contaminated wounds in an animal model[146]. Using the presence of pus as the sole criterion for wound infection, they found that 73% of wounds that had been contaminated prior to closure with silk were infected at one week in comparison with 23% of wounds that had been closed with subcuticular Dexon sutures ($p < 0.05$).

The correct management of surgical dead space, particularly in the setting of gross contamination or infection, is controversial. Condie and Ferguson found that layered closure improved healing of contaminated abdominal wounds in a dog model[147]. In contrast, de Holl et al. found an increased rate of infection after dead space closure in an animal model[148]. A meta-analysis of 875 patients was done to assess dead space wound closure after cesarean delivery; it demonstrated 34% fewer wound complications with use of a layered closure, compared with the rate associated with closure of the skin only, when >2 cm of subcutaneous adipose tissue was present[149].

The proper management of dead space in orthopaedic patients has not been clearly defined. Proper removal of infected or necrotic tissue, thorough irrigation, and appropriate antibiotic treatment improve wound-healing. There is evidence that subcuticular wound closure with monofilament sutur minimizes tissue ischemia and is associated with decreased bacterial contamination.

Surgical Dressing and Wound Care

Wound dressings assist with healing by acting as a physical barrier to bacteria, immobilizing or splinting the wound to protect it from subsequent injury, helping with hemostasis (i.e., pressure dressings), reducing dead space, and minimizing pain. Multiple studies have shown that, with the use of occlusive dressings, both re-epithelialization and subsequent collagen synthesis are two to six times faster than they are in wounds exposed to air[150-154]. On a cellular level, dressings assist wound-healing by creating a hypoxic wound environment wherein fibroblasts proliferate and angiogenesis occurs more rapidly. The host's defenses are thought to be improved under an occlusive dressing, and the creation of this hypoxic, acidic environment is thought to slow the growth of normal skin pathogens. Dressings act as a physical barrier to reduce the migration of bacteria into the wound[150]. Hutchinson and McGuckin, in a systematic review of 111 studies, found that the rate of infection under occlusive dressings was lower than that under nonocclusive dressings (2.6% compared with 7.1%)[155]. Studies comparing nonbiologic occlusive dressings have suggested that, although their physical characteristics differ, there does not appear to be any clear benefit of one occlusive dressing over another. In a recent review of open and occlusive dressings, the authors recommended that surgical wounds be covered with a three-layer dressing[156]. The first layer, placed directly on the wound, should be a non-adhering, hydrophilic dressing such as Adaptic (Johnson and Johnson, New Brunswick, New Jersey) or Xeroform (Sherwood Medical Industries, Markham, Ontario, Canada). An absorptive layer (i.e., gauze) would be placed on the first layer. The third layer would be an occlusive material to adhere the dressing to the skin.

The proper timing of dressing removal is also controversial. Studies of clean and clean-contaminated wounds showed no difference in infection rates according to whether the dressing was removed on the first postoperative day or at the time of suture removal[157,158]. After the dressing is removed, the wound may be cleaned with tap water or saline solution, but antiseptics such as hydrogen peroxide should be avoided. Showering may commence after wound epithelialization without an increased risk of infection[150].

A variety of creams, ointments, and solutions have been advocated as means of propagating wound epithelialization. Cooper et al. evaluated the toxicity of several antimicrobial agents and found povidone-iodine to be significantly more toxic to fibroblasts than other agents ($p < 0.05$)[102]. Kramer showed a detrimental effect of povidone-iodine on wound-healing[103]. Triple antibiotic ointment was shown to increase re-epithelialization by 25% in an animal model[159]. In a prospective, randomized, controlled trial evaluating 426 uncomplicated wounds, the infection rates in the groups treated with bacitracin ointment (six of 109, 5.5%) or triple antibiotic ointment (five of 110, 4.5%) were lower than those in the groups treated with silver sulfadiazine (twelve of ninety-nine, 12.1%) or petroleum (nineteen of 108, 17.6%) ($p = 0.0034$)[160]. Broad-spectrum ointments provide occlusion and increase epithelialization while the wound heals.

The majority of evidence-based reports on wound dressings have been published in the plastic surgery and dermatology literature. Current recommendations for the management of uninfected surgical wounds include the use of a three-layered surgical dressing. The use of a triple antibiotic ointment can be followed by application of a nonadherent, hydrophilic layer. The second layer should be absorptive, and the final layer should be occlusive to contain the underlying physiologic milieu. The dressing may be removed as early as the first postoperative day, and the wound may be gently cleaned with water or saline solution (Table IV).

Operating Room

One area of infection prevention that is often overlooked is the operating room itself. Several studies have shown that improvements in airflow and ultraviolet lighting reduce not only bacterial counts but also rates of surgical site infection. A cohort study by Knobben et al.[161] demonstrated that, compared with use of conventional airflow systems, use of a laminar-flow operating theater significantly decreased the rates of bacterial wound contamination ($p = 0.001$), prolonged wound discharge ($p = 0.002$), and superficial infection of the surgical site ($p = 0.004$). A retrospective study by Gruenberg et al. showed that conducting spinal fusions in vertical laminar-flow operating rooms dramatically reduced the rate of wound infections (zero of forty patients) compared with that following procedures conducted in conventionally ventilated operating rooms (eighteen [13%] of 139 patients, $p < 0.017$)[162]. Hansen et al. sampled operative fields in laminar-flow rooms and found them to be, on the average, twenty times less contaminated than operative fields in comparable rooms without laminar flow (Table III)[163].

The use of ultraviolet light as a means of reducing the airborne bacterial burden and possibly the rate of wound infections has also been studied. Multiple basic-science studies have shown that ultraviolet light decreases the numbers of colony-forming units[164,165]. Berg et al. found ultraviolet light to be even more effective than a laminar-flow ventilation system in decreasing airborne bacterial load[166,167]. Modern high-volume exchange in operating rooms has resulted in equivalent levels of colony-forming units and decreased the benefit of ultraviolet light.

We are not aware of any Level-I clinical data on operating-room issues of clothing type, body exhaust, number of personnel, and conversation in operating rooms. Several well-performed basic-science studies have demonstrated increases in colony-forming units in operating rooms, which might be extrapolated as increasing the risk of deep infection. Critical wound contamination most likely results from airborne bacteria or residual bacteria on the skin after cleaning.

The greatest source of airborne bacteria is the operating-room personnel, with ears and beards being the two areas most likely to shed bacteria[168]. Bethune et al. found that men shed a greater number of bacteria per minute than postmenopausal women, and premenopausal women shed even fewer bacteria[169]. The number of bacteria shed by operating-room personnel can be decreased by using air exhaust systems or completely covering ears and beards[168]. If operating-room-personnel exhaust systems are not feasible, the dress of the personnel can influence the number of colony-forming units grown on culture of specimens obtained in operating rooms. The use of wraparound gowns and synthetic gowns decreases the number of colony-forming units compared with that associated with the use of cotton gowns or operating-room clothing[170]. Blom et al. recommended the use of nonwoven disposable drapes or woven drapes with an impermeable layer below them for surgical draping[171]. Ritter indicated that the average number of colony-forming units in an operating room was increased from 13.4 to 24.8 when the doors were left open and that intermittent opening of doors did not significantly decrease the number of colony-forming units compared with that measured when the doors were left open[172]. Implants have also been shown to be associated with a higher rate of positive cultures if left outside their packaging in the operating room for more than two hours[173].

In addition to the above prophylactic measures, there is excellent evidence that surgical site infection can be decreased by close control of perioperative glucose levels, especially in patients with diabetes[174-179]; by maximizing patient oxygenation in the first twenty-four hours perioperatively[180-183]; and by maintaining patient normothermia in the perioperative period (Table III)[184]. Forty-four hospitals reported data on more than 35,000 patients during a trial to maximize control of glucose, oxygenation, and normothermia in the postoperative setting. Over the course of the study, the infection rate decreased 27%, from 2.3% to 1.7%. Thus, a surgical infection occurred in 200 fewer patients in these hospitals.

Overview

There are significant data that can help surgeons to decrease the risk of perioperative surgical site infections. We reviewed the best available literature and made recommendations in an attempt to help orthopaedic surgeons to minimize surgical site infections in their patients.

Appendix

Tables listing important evidence-based articles on preoperative antibiotics, surgical scrubs, and use of surgical drains; a table presenting the Gustilo and Anderson classification system for open fractures; and a table listing the activities of antiseptic agents are available with the electronic versions of this article, on our web site at jbjs.org (go to the article citation and click on "Supplementary Material") and on our quarterly CD-ROM (call our subscription department, at 781-449-9780, to order the CD-ROM).

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