Prevention of Periprosthetic Joint Infection

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Introduction

Prosthetic joint infection (PJI) is a relatively rare but devastating complication following total joint replacement. While PJI may occur at any time following joint replacement surgery, the majority are diagnosed within the first 2 years of the index procedure [1, 2]. The diagnosis of a PJI has significant effects beyond the morbidity associated with infection treatment. PJI has been associated with a mortality rate from 2.7 to 18 %, which is far in excess of the mortality rates associated with primary joint replacement and aseptic revision surgery. [3–8]. Furthermore, the subsequent cost of treating PJI incurred by both the patient and the health care system is approximately 4 times the cost of a primary total joint arthroplasty (TJA) [4, 5, 7].

Given the impending changes in population demographics, the burden of treating these difficult infections will only increase over time. Projections by Kurtz et al. suggest a 673 % increase in primary total knee arthroplasties and a 174 % increase in primary total hip arthroplasties performed annually in the United States by the year 2030. Dramatic increases are also expected in the number of revision arthroplasties performed annually. [9]. Given the expanding size of the population at risk, every effort must be made to implement effective infection prevention strategies.

There are multiple factors associated with the development of PJI, including patient-related factors, surgical factors, environmental factors, and the emergence of drug-resistant microorganisms. Effective prevention strategies must address these factors in the preoperative, intraoperative, and postoperative settings. The purpose of this chapter will be to review known PJI prevention strategies, with a special emphasis on *Staphylococcus aureus* screening and decolonization.

Risk Factors

Identifying at-risk patients is the first step in medical optimization and targeted risk reduction. Preoperative patient risk factors for infection are outlined in Table 3.1. [1–3, 10–12]:

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Table 3.1 Patient risk factors

Non-modifiable risks
• Low income patients (Medicaid)
• Age over 75 years
• Males
• Systemic malignancy
• ASA score >2
• Prior joint surgery (i.e., revisions, prior fracture surgery)
• National Nosocomial Infections Surveillance risk index >1
• Lower volume hospitals/surgeons
Potentially modifiable risks
• Morbid obesity
• Longer duration of surgery (>210 min)
• Simultaneous bilateral procedures
• Preoperative stay >2 days
• Longer hospital stay (>5 days)
• Blood transfusion
• Postoperative wound complications

Preoperative Infection Prevention Strategies

Medical optimization prior to the operation is crucial to the success of the procedure. Basics of optimization include reducing the insult of other comorbidities, improving nutrition, smoking cessation, weight management, blood sugar management, and *S. aureus* screening and decolonization [13, 14].

The authors recommend that all patients have a preoperative medical evaluation for general health optimization. Chronic medical conditions, especially cardiopulmonary issues, should be identified and optimized preoperatively. Remote site infections (e.g., poor dentition and urinary tract infection) should be investigated and treated prior to the procedure.

Nutritional status is often neglected during the preoperative evaluation; however, ensuring proper nutrition is quite important. Malnourished patients have demonstrated a five- to sevenfold increased risk in developing major wound complications [15]. Preoperative screening for malnutrition should be employed in patients felt to be at risk based on the history and physical examination. Several laboratory tests have been proven to predict postoperative complications[16, 17]. Indicators of possible malnutrition include: body mass index (BMI) <20, total cholesterol <160 mg/dL, total lymphocyte count <1,500 cells/mm^3, transferrin <200 mg/dL, and albumin <3.5 mg/dL. These tests may be collected at the same time as other routine preoperative labs. When diagnosed preoperatively, malnutrition should be treated under the guidance of the appropriate medical specialist until corrected. In the postoperative period, proper nutrition should be encouraged. Every attempt should be made to minimize the period of restricted oral intake. Enteral supplements, protein supplements, and multivitamins should be considered during the postoperative period for at-risk patients.

Smoking cessation should be highly encouraged as another means to optimize patients prior to joint replacement surgery. Carbon monoxide and other components of tobacco smoke result in decreased blood flow to the surgical site, decreased aerobic metabolism and oxygenation, and increased local platelet aggregation. Furthermore, restricted circulation decreases the local delivery of the humoral and cellular mechanisms of immunity to the surgical site [18]. In addition to the risks of PJI, smoking has been shown to cause accelerated bone density loss, increased risk of hip fracture, lumbar disk disease, increased incidence of low back pain, increased risk of wrist fracture, and delayed fracture healing [17, 19]. Smoking cessation at least 6 months prior to the orthopedic procedure is recommended [17]. Proven techniques that promote prolonged cessation include counseling, self-help groups, nicotine replacement therapy, and physician counseling. Pharmacologic agents, such as bupropion and varencicline, are effective methods of increasing the likelihood of smoking cessation, especially when combined with the above-mentioned modalities [18].

Obese patients have a significant increase in periprosthetic joint infection risk compared to those with a normal BMI [20]. Obesity is defined as a BMI >30 kg/m^2. Postoperative complication rates increase with larger BMI. Obese patients incur significant perioperative risks involving the cardiac and pulmonary systems as a result

of increased cardiac work, decreased lung compliance, and decreased functional residual capacity. Obesity is felt to increase the risk for PJI in a multifaceted manner. First, obesity may significantly distort the local anatomy and add greatly to the difficulty, and therefore the duration, of the operative procedure. Next, poorly vascularized subcutaneous fat and the resultant postoperative dead space from the added surgical dissection contribute to both hematoma and seroma formation, which are known risks for infection. One representative study demonstrated a significantly elevated complication rate in patients with a BMI ≥40 when compared to patients with BMI <40 [21]. Although no absolute "cutoff" value with respect to BMI is utilized, the authors feel that every attempt should be made to reduce the BMI to <40 preoperatively, while maintaining appropriate overall nutritional status.

Strict perioperative glycemic control is becoming a better recognized means of reducing the risk for PJI. Controlled glycemic levels provide patients with significant risk reductions when compared to those with uncontrolled levels in areas beyond infection. These include length of stay, stroke, myocardial infarction, postoperative hemorrhage, urinary tract infection, and pneumonia. When properly controlled, patients with diabetes can lower their risk of infections to levels near those without diabetes [22].

S. aureus Screening and Decolonization

S. aureus is the leading cause of orthopedic surgical site infection (SSI), and the prevalence of methicillin-resistant S*taph aureus* (MRSA) SSI is increasing in community and healthcare settings [23–28]. The two strains of *S. aureus* responsible for these infections are methicillin-sensitive *Staph aureus* (MSSA) and MRSA. SSIs due to MRSA have been associated with increased morbidity, morality, and increased length of hospital stay [29].

S. aureus resides on the skin surfaces in one-third of the general population who remain asymptomatic [30]. Studies have demonstrated that MSSA/MRSA can be detected in moist areas of the body such as nares, throat, axilla, and perineum. Nasal screening identified 66 % of the carriers; while combining nasal and perineal swabs gave the best two-site combination (82 %). [31]. Since the anterior nares are the site of highest colonization, this is the traditional site for screening tests [32]. New developments such as real time PCR offer rapid, sensitive, and specific strain identification of *S. aureus* [33]. Nasal carriage of *S. aureus* is strongly associated with skin colonization and such patients are 2–9 times more likely to acquire SSI. *S. aureus* nasal carriage was the only independent risk factor for SSI following orthopedic implant surgery in several studies [34–37].

One of the strategies that has shown a great deal of promise is the use of staphylococcal decolonization to eradicate the nasal/skin colonization of *S. aureus* (MSSA, MRSA) to prevent SSI. Surveys administered in the United States and Europe show that decolonization is being attempted frequently in various settings. [38, 39]. Many agents and various approaches have been used to eradicate *S. aureus* colonization. Most strategies result in only short-term decolonization. Eradication of nasal and skin carriage at the time of surgery would seem to be a logical approach to reduce the risk for postoperative staphylococcal infection [40].

The most common and well-studied decolonization protocol used selectively in colonized patients is the use of topical intranasal mupirocin ointment twice daily and chlorhexidine body washes for 5 days immediately prior to surgery. In addition, patients who are colonized with MRSA receive perioperative intravenous vancomycin prophylaxis in place of, or in addition to, a first-generation cephalosporin antibiotic [41].

A systematic review inclusive of retrospective and prospective studies that evaluated the effect of *S. aureus* decolonization in orthopedic patients showed a significant reduction in SSI. The prospective data conducted at our institution (N.R.) performed two analyses and compared the intervention group with two different control groups. In the first analysis, none of the carriers in the intervention group developed SSI during a 2-year

follow-up period, whereas 19 patients in the concurrent control group developed SSI (0 % vs. 3.3 %). In the second analysis, screening and selective decolonization appeared to be associated with a decrease in the overall SSI rate compared to that during the pre-intervention period (1.2 % vs. 2.7 %)—again approximating previous findings (1.4 % vs. 2.7 %). Importantly, the protocol reduced *S. aureus* infection without increasing the rate of infections due to other pathogens [41]. The effect of screening and decolonization on SSI in orthopedic patients is outlined in Table 3.2.

Overall reduction in SSI was significant when the studies were aggregated, as implementation of decolonization was associated with lower infection rates [41–49]. At our institution (N.R.), the efficacy of the decolonization protocol in eradication of MSSA colonization was significant ($p<0.001$) while the eradication of MRSA colonization approached statistical difference (5/5, $p=0.063$) (unpublished data).

The cost-effectiveness using economic models demonstrates that screening and decolonization of *S. aureus* in orthopedic patients, specifically in TJA patients, would be an economically dominant strategy [41, 43, 47, 49–53]. Mupirocin and chlorhexidine are safe and cost-effective agents. The protocol is simple, practical to implement, and achieves a high rate of compliance. The authors believe that all patients scheduled for total joint replacement should be screened for the presence of *S. aureus*, and patients screened as positive for colonizations should be treated accordingly.

Intraoperative Infection Prevention Strategies

In the operating room, lowering the risk for PJI requires appropriate skin preparation for bacterial reduction at the surgical site. Preoperative hair removal does not have significant data to support its use and some surgeons advocate against it, citing a potentially increased risk of SSI. However, the use of clippers, in which the cutting edges do not touch the skin, demonstrates a reduction in postoperative infection rates and relative risk for infection when compared to skin shaving with a razor. It is important to note that hair reduction should be performed immediately prior to, rather than the night before, the planned surgical procedure [54–56]. The ideal skin preparation for sterility requires a scrub that will have both antimicrobial and anti-spore activities with residual activity well after the time of application. Common agents used for skin preparation include povidone-iodine (Betadine), alcohol, ChloraPrep® (CareFusion Corporation, San Diego, CA), and DuraPrep™ (3M Corporation, Saint Paul, MN).

Alcohol has the fastest microbial reduction and may increase the antiseptic activity of povidone-iodine solutions if used jointly. However, alcohol does not have residual activity and allows rebound microbial growth [57]. Betadine is effective as paint, but fails to provide adequate drape adherence in order to prevent lift-off. DuraPrep™ is as effective as Betadine in bacterial reduction and is far superior in terms of drape adherence than both Betadine and ChloraPrep [57, 58].

Draping is a multistep process that involves many different materials. Plastic adhesive tape drapes do not permit vertical migration of bacteria compared to the tenfold increase that cloth drapes allow. Additionally, use of iodine-impregnated drapes reduces the rate of recolonization when combined with plastic adhesive drapes. While literature supports the reduction in postoperative wound contamination in critical care and obstetrics, orthopedic specific literature does not show any decrease in wound infection rate [57].

The greatest source of airborne bacteria comes from operating room personnel, and therefore traffic should be reduced to a minimum [59, 60]. Surgical attire for the operating room can greatly reduce the airborne bacterial load by covering hair, ears, and fully covering beards. Wrap around gowns and personal exhaust systems are associated with reduced numbers of colony-forming units when compared to standard cotton gowns or surgical attire [61]. Proper surgeon preoperative hand scrubbing is another means of reducing the bacterial load within the surgical environment. While the traditional scrub brush with a povidone-iodine or

Table 3.2 Studies evaluating *Staphylococcus aureus* decolonization in TJA

Author (year)	Country/design	Patient population	Sample size	Controls	% Colonized	Patients decolonized	Protocol	% Reduction in SSI	*P* value
Rao et al. (2011) [19]	US/prospective	TJA	3,025	Concurrent Historic	MSSA 22 % MRSA 3 %	Positive nasal screens	2 % Mupirocin × 5 days Chlorhexidine × 5 days	76.9 % reduction in SSI	0.009
Kim et al. (2010) [20]	US/prospective	TJA/spine sports	7,019	Historic	MSSA 22.6 % MRSA 4.4 %	Positive nasal screens	2% Mupirocin × 5 days Chlorhexidine × 5 days	81.3 % reduction in SSI	0.009
Rao et al. (2008) [21]	US/prospective	TJA	1,966	Concurrent Historic	MSSA 23 % MRSA 3 %	Positive nasal screens	2 % Mupirocin × 5 days Chlorhexidine × 5 days	200 % reduction in SSI	0.016
Sankar et al. (2005) [22]	UK/prospective	TJA	395	Historic	N/A	Positive nasal, groin, axilla wound	Mupirocin/povidone-iodine/triclosan	200 % reduction SSI	0.05
Wilcox et al. (2003) [23]	UK/prospective	Orthopedic patients with metal prosthesis and/fixation	2,178	Historic	MSSA 27 % MRSA 38 %	All patients	Mupirocin × 5 days Triclosan × 1 day	149 % reduction MRSA SSI	0.001
Hadley et al. (2010) [24]	US retrospective	TJA	2,058	Concurrent	MSSA 21.4 % MRSA 3.5 %	Positive screens	2 % Mupirocin × 5 days Chlorhexidine × 1 day	12.5 % reduction of SSI	0.809
Hacek et al. (2008) [25]	US/retrospective	TJA	1,495	Historic	*S. aureus* 24.5 %	Positive nasal screens	2 % Mupirocin × 5 days Chlorhexidine × 1 day	75.3 % reduction of SSI	<0.1
Price et al. (2008) [26]	US/retrospective	Elective orthopedic patients	284	None	MSSA 28.5 % MRSA 1.8 %	Positive nasal screens	2 % Mupirocin × 5 days	200 % reduction of SSI	NA
Nixon et al. (2006) [27]	UK/retrospective	Elective and trauma orthopedic patients	5,594	Historic	MRSA elective 1.3 % Trauma 3.8 %	Positive nasal screens	2 % Mupirocin × 5 days	Trauma 56 % reduction of MRSA	0.035
							Triclosan × 5 days	SSI elective 70 % reduction of MRSA SSI	0.06

TJA total joint arthroplasty, *MRSA* methicillin-resistant *Staphylococcus aureus, MSSA* methicillin-sensitive *Staphylococcus aureus*, *SSI* surgical site infection, *NA* not available, *UK* United Kingdom, *US* United States of America

chlorhexidine is effective, proper procedure regarding the actual wash is not strictly followed. Newer, scrubless skin preparation options demonstrate better adherence to proper protocol, take less time, and have better antibacterial efficacy with prolonged use [62–64].

Double-gloving is recommended as it reduces the risk of perforation of the inner glove and subsequent surgical site contamination. Routine changing of the outer gloves during the procedure further reduces the risk of inner glove perforation and is an effective way to reduce bacterial contamination prior to handling of the implant [65, 66].

Laminar airflow, in which air filters remove particles >0.3 μm, demonstrates decreased bacterial wound contamination when compared to conventional air flow [67]. When controlled for antibiotic use, laminar airflow has been associated with lower prevalence of infection. Both Charnley and Ritter demonstrated successful infection reduction after implementation of laminar airflow when compared to operations without laminar airflow. The success is dependent upon patient positioning, personnel location, surgery type (hip or knee), and direction of flow. Knee surgery appears to benefit less than hip surgeries. The effect of the directed air decreases when personnel move in the way of the air flow. Further, cost may be prohibitive as retro-fitting and operating may cost a significant amount of money [68, 69]. The relative benefit of laminar airflow remains a controversial topic.

Ultraviolet (UV) light is another method of minimizing the risk of intraoperative wound contamination. Several studies evaluating the effectiveness of UV light have shown a decrease in the rate of infection compared to operating rooms without ultraviolet lights. UV lights are of low cost, low maintenance, and are relatively safe with proper protection equipment that can contribute to lower infection rates. However, there are concerns regarding UV lights, such as overexposure, severe conjunctivitis, blindness after prolonged exposure, and superficial erythema [68].

Prolonged operative time has been identified as a significant risk factor for the later development of PJI [57, 70, 71]. Although the exact time at which an operation becomes "prolonged" is impossible to determine, there is certainly never a benefit to a more lengthy procedure. In total knee replacement, an operative time greater than 120 min is a significant risk factor for infection. The association between operative time and infection risk is likely multifactorial, as it may be a proxy for other issues that predispose to complications, such as hypothermia, increased local tissue damage related to added dissection and/or prolonged retraction, and greater blood loss. Every effort should be made to maximize surgical efficiency.

The risk of PJI is increased for patients requiring allogeneic blood transfusion [72–74]. A comprehensive blood management plan is part of any PJI risk reduction strategy and involves treating preoperative anemia, minimizing intraoperative blood loss, and avoidance of postoperative transfusion unless truly indicated [74].

Prophylactic Antibiotics

The benefit of timely and appropriate prophylactic antibiotics prior to total joint replacement is unquestioned. Henley used a prospective randomized double-blinded study of general orthopedic procedures showing prophylactic antibiotics had a 1.6 % infection rate compared to the placebo group of 4.2 % [75]. Prophylactic antibiotics reduce the absolute risk and relative risk when compared to the same procedure without antibiotic prophylaxis [76, 77]. For the antibiotics to be effective, they must target the appropriate organism. Most sources of bacterial contamination arise from the patient's skin or airborne sources. In primary joint arthroplasties, *Staphylococcal* and *Streptococcal* species are the primary targets. A long half-life, excellent tissue penetration and effectiveness against *Staphylococcal* and *Streptococcal* organisms make first-generation cephalosporins the antibiotic of choice for the vast majority of orthopedic procedures, including total joint replacement [12, 78–81]. Vancomycin, either alone or in combination with a first-generation cephalosporin, should be used for MRSA-colonized patients [57]. Although many patients

self-report a history of "penicillin allergy," rates of true cross-reactivity with penicillin and cephalosporin and the risk for subsequent anaphylaxis vary from 0.0001 to 0.1 % [82]. Patients should be specifically tested for a true cephalosporin reaction in the preoperative period whenever possible in order to both avoid the overuse of vancomycin and realize the efficacy of the cephalosporin. Patients with confirmed beta-lactam allergy should receive vancomycin or clindamycin as the alternative method of antibiotic prophylaxis.

Cefazolin should be dosed based on the patient's body mass: 1 g for weight <80 kg, 2 g for weight >80–120 kg, and 3 g for weight >120 kg. It is redosed every 2–5 h. Vancomycin is given at a dose of 15 mg/kg and is redosed every 6–12 h. Clindamycin is standardized at 600 mg per dose and redosed every 3–6 h. The antibiotics should be administered and completed within 1 h of incision. Subsequent doses should be administered if the length of the procedure exceeds the half-life of the drug, or if greater than 70 % of circulating blood volume is lost [57, 59]. The postoperative duration of antibiotic administration should be confined to 24 h. There is no significant difference in infection prevention when comparing postoperative antibiotics for 24 h vs. 3–14 days. Further, minimizing the length of postoperative antibiotic duration reduces the cost of healthcare [83–87].

Antibiotic-impregnated bone cement is a means of local antibiotic delivery. Using cement as a delivery mechanism allows for local elution of the majority of the antibiotics in the first 9 weeks [88]. Local delivery allows for tissue antibiotic levels far superior to those seen after systemic administration alone [69]. The beneficial effect is therefore in the reduction of implant colonization from intraoperative contamination. Antibiotic cement used at the time of arthroplasty is unlikely to confer any risk reduction for the development of late hematogenous infection. When combined with systemic antibiotics, antibiotic-impregnated cement for cemented total hip arthroplasty has shown a reduction in revision rates for infection as well as all-cause revisions. [89, 90].

Additional Intraoperative Infection Prevention Strategies

Intraoperative irrigation removes debris, blood clots, and reduces bacterial contamination. There is no absolute consensus as to the use of pulsatile lavage rather than bulb lavage. While the higher pressure of pulse lavage does remove a larger bacterial load than bulb lavage, it also has an increased rate of deep bacterial seeding in bone. High pressure may also increase muscle damage and decrease particulate removal when compared to bulb irrigation [91, 92]. Normal saline and soap solutions remove significantly more bacteria from the surgical field when compared to antibiotic-mixed irrigation. Further, antibiotic solution has potential for tissue toxicity and has evidence of wound-healing problems [93, 94]. While there is strong evidence that soap irrigation is superior to antibiotic-impregnated or normal saline solution, there are no strong human studies to indicate the routine addition of antibiotics to irrigation solution. In routine orthopedic procedures, low-to-intermediate lavage is adequate and high pressure lavage should be reserved for severely contaminated and/or open fractures in which treatment is delayed [59].

While the use of drains may theoretically reduce the risk for postoperative hematoma formation, there is no current literature to support the use of drains in routine primary arthroplasties. Multiple studies demonstrate no difference in rates of infection, wound complications, thromboembolic complications, hospital stay, or hematoma formation with or without the use of a postoperative suction drain. However, if a drain is used, it should be removed within 24 h of the procedure in order to minimize the risk of PJI [95, 96].

No evidence is available to support a specific method of wound closure that reduces the rates of infection or wound complications in routine orthopedic procedures. Occlusive surgical dressings provide protection from bacteria, faster re-epithelialization, faster collagen synthesis, and create an environment in which fibroblast and angiogenesis occur [97, 98]. Current recommendations based on literature include a three-layer dressing.

The first layer is directly over the wound and is a non-adherent hydrophilic dressing followed by an absorptive layer of gauze. The third and outer later is the occlusive layer that adheres the dressing to the skin [96, 99].

Postoperative Infection Prevention Strategies

The elevated risk for venous thromboembolism (VTE) following total joint replacement requires the use of a multimodal VTE risk reduction strategy which often requires some type of chemoprophylaxis. Potent anticoagulants are a major contributor to hematoma formation in the postoperative period. Subsequent infection at the site of hematoma is a significant risk for PJI [100]. Parvizi et al. found that excessive anticoagulation (INR >1.5) and the development of a hematoma had a significant increase in periprosthetic infection rate [101]. In another study, operative evacuation of a postoperative hematoma significantly increases the risk for the development of a PJI and the need for further surgery [102].

The routine use of prophylactic antibiotics prior to invasive procedures remains controversial. While no definitive evidence is available to show the association between dental procedures and periprosthetic joint infection, the AAOS recommends antibiotic prophylaxis for patients who undergo dental procedures after having joint arthroplasties [103]. Current antibiotics for dental procedures are given 1 h prior to the procedure. Drug options include 2 g of amoxicillin, 2 g of cephalexin, or 600 mg of clindamycin. For any genitourinary or gastrointestinal procedures, 750 mg of ciprofloxacin is recommended 1 h before the procedure.

Conclusion

PJI is a devastating complication following total joint replacement that leads to excess morbidity, mortality, and cost. This chapter has outlined effective prevention strategies that may be utilized in all phases of perioperative care. A multifaceted approach to the patient undergoing total joint replacement will have the greatest positive effect. Further study will be needed to identify and share "best practice" models that might be emulated to lower the PJI risk for all patients.

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