

# Prevention of Periprosthetic Joint Infections of the Hip and Knee

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## Abstract

Periprosthetic joint infection (PJI) is a rare but devastating complication of arthroplasty. Research has been dedicated to minimizing the incidence of PJI, leading to the development of a comprehensive perioperative approach. Multiple preoperative, intraoperative, and postoperative factors can increase patient risk. From medical management and skin sterilization to wound sterility and blood management, multiple issues must be considered in a well-rounded prevention protocol. In this literature review, we consolidate the current information that orthopedic surgeons can use to minimize PJI after total knee arthroplasty and total hip arthroplasty.

Nearly 2% of patients who undergo total knee arthroplasty (TKA) or total hip arthroplasty (THA) develop a periprosthetic joint infection (PJI) within 20 years of surgery, and 41% of these infections occur within the first 2 years.<sup>1</sup> PJI is the most common cause of TKA failure and the third leading complication of THA.<sup>2</sup> The estimated total hospital cost of treating PJI increased from \$320 million in 2001 to \$566 million in 2009, which can be extrapolated to \$1.62 billion in 2020.<sup>3</sup> By 2030, the projected increase in demand for TKA and THA will be 673% and 174% of what it was in 2005, respectively.<sup>4</sup> Treatment of PJI of the knee is estimated to cost 3 to 4 times more than a primary TKA, and the cost of revision THA for PJI is almost \$6000 more than that of revision TKA for PJI.<sup>3</sup>

In this article, we review the numerous preoperative, intraoperative, and postoperative methods

of decreasing PJI incidence after total joint arthroplasty (TJA).

## Preoperative Risk Prevention

### Medical Comorbidities

Preoperative medical optimization is a key element in PJI prevention (**Table 1**). An American Society of Anesthesiologists classification score of 3 or more has been associated with doubled risk for surgical site infections (SSIs) after THA.<sup>5</sup> Autoimmune conditions confer a particularly higher risk. In a retrospective double-cohort study of 924 subjects, Bongartz and colleagues<sup>6</sup> found that, compared with osteoarthritis, rheumatoid arthritis tripled the risk of PJI. Small case series originally suggested a higher risk of PJI in patients with psoriasis,<sup>7,8</sup> but more recent studies have contradicted that finding.<sup>9,10</sup> Nevertheless, psoriatic plaques have elevated bacterial counts,<sup>11</sup> and planned incisions should circumvent these areas.

Diabetes mellitus is a clear risk factor for PJI.<sup>12-16</sup> Regarding whether preoperative glucose control affects risk, findings have been mixed. Mraovic and colleagues<sup>17</sup> showed preoperative hyperglycemia to be an independent risk factor; Jämsen and colleagues,<sup>15</sup> in a single-center analysis of more than 7000 TJAs, suggested preoperative blood glucose levels were not independently associated with PJI; and Iorio and colleagues<sup>16</sup> found no association between surgical infections and hemoglobin A<sub>1c</sub> levels.

TJA incidence is higher in patients with chronic kidney disease (CKD) than in the general population.<sup>18</sup> Dialysis users have a post-THA PJI rate as high as 13% to 19%.<sup>19,20</sup> Early clinical data suggested that outcomes are improved in dialysis users who undergo renal transplant, but this finding recently has been questioned.<sup>19,21</sup> Deegan and colleagues<sup>22</sup> found an increased PJA rate of 3.5% even in low-level CKD (stage 1, 2, or 3), but this may be confounded by the increased association

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of CKD with other PJI-predisposing comorbidities.

Given a higher incidence of urinary tract infections (UTIs) among patients with PJI, some surgeons think UTIs predispose to PJIs by hematogenous seeding.<sup>12,23,24</sup> Symptomatic UTIs should be cleared before surgery and confirmed on urinalysis. Obstructive symptoms should prompt urologic evaluation. As asymptomatic pyuria and bacteriuria (colony counts,  $>1 \times 10^5/\text{mL}$ ) do not predispose to PJI, patients without symptoms do not require intervention.<sup>25,26</sup>

Past history of malignancy may also have a role in PJI. In a case-control study of the Mayo Clinic arthroplasty experience from 1969 to 1991, Berbari and colleagues<sup>1</sup> found an association between malignancy and PJI (odds ratio, 2.4). They theorized the immunosuppressive effects of cancer treatment might be responsible for this increased risk.

### Immunocompromising Medications

Immunocompromising medications are modifiable and should be adjusted before surgery. Stopping any disease-modifying antirheumatic drug (DMARD) more than 4 weeks before surgery is not recommended.<sup>27</sup>

Corticosteroid use can lead to immunosuppression and increased protein catabolism, which impairs soft-tissue healing. To avoid flares or adrenal insufficiency, however, chronic corticosteroid users

should continue their regular doses perioperatively.<sup>28</sup> On the day of surgery, they should also receive a stress dose of hydrocortisone 50 to 75 mg (for primary arthroplasty) or 100 to 150 mg (for revision arthroplasty), followed by expeditious tapering over 1 to 2 days.<sup>29</sup>

DMARDs are increasingly used by rheumatologists. One of the most effective DMARDs is methotrexate. Despite its immunocompromising activity, methotrexate should be continued perioperatively, as stopping for even 2 days may increase flare-related complications.<sup>30</sup> Hydroxychloroquine can be continued perioperatively and has even been shown, by Johnson and Charnley,<sup>31</sup> to prevent deep vein thromboses. Sulfasalazine can also be continued perioperatively—but with caution, as it may elevate international normalized ratio (INR) levels in patients receiving warfarin.<sup>29</sup>

Most other DMARDs should be temporarily discontinued. Leflunomide and interleukin 1 antagonists, such as anakinra, should be stopped 1 to 2 days before surgery and restarted 10 to 14 days after surgery.<sup>29</sup> Rituximab should be stopped 1 week before surgery and restarted 10 to 14 days after surgery. Tumor necrosis factor  $\alpha$  inhibitors should be discontinued for 2 half-lives before and after surgery.<sup>32</sup> Etanercept has a half-life of 3 to 5 days; infliximab, 8 to 10 days; and adalimumab, 10 to 13 days. Most surgeons schedule surgery for the end of a dosing cycle and discontinue these biologic agents for another 10 to 14 days after surgery.

### Metabolic Factors

Obese patients are susceptible to longer surgeries, more extensive dissection, poorly vascularized subcutaneous tissue, and higher requirements of weight-adjusted antibiotic dosing.<sup>13</sup> Body mass index (BMI) of 40 kg/m<sup>2</sup> or more (morbid obesity) and BMI over 50 kg/m<sup>2</sup> have been associated with 9 times and 21.3 times increased risk of PJI, respectively.<sup>13,14</sup> Delaying surgery with dietary consultation has been suggested,<sup>33,34</sup> and bariatric surgery before TKA may decrease infection rates by 3.5 times.<sup>35</sup>

Nutritional markers are considered before arthroplasty. According to most laboratories, a serum transferrin level under 200 mg/dL, albumin level under 3.5 g/dL, and total lymphocyte count under 1500 cells/mm<sup>3</sup> indicate malnourishment, which can increase the incidence of wound complications by 5 to 7 times.<sup>36</sup> Patients should also have sufficient protein, vitamin, and mineral supplementation, particularly vitamins A and C, zinc, and copper.<sup>37</sup>

**Table 1. Preoperative Factors Associated With Increased Risk of Periprosthetic Joint Infection**

American Society of Anesthesiologists score $\geq 3$
Rheumatoid arthritis
Psoriatic plaques
Hyperglycemia
Chronic kidney disease
Urinary tract infections
Malignancy
Immunocompromising medications
Obesity
Malnutrition
Tobacco use
Alcoholism
Methicillin-resistant <i>Staphylococcus aureus</i> decolonization

Smokers who cease smoking at least 4 to 6 weeks before surgery lower their wound complication rate by up to 26%.<sup>38,39</sup> When nicotine leaves the bloodstream, vasodilation occurs, oxygenation improves, and the immune system recovers.<sup>39</sup> Studies have found more SSIs in patients who abuse alcohol,<sup>40</sup> and numerous authors have confirmed this finding in the arthroplasty population.<sup>24,41,42</sup> Alcohol inhibits platelet function and may predispose to a postoperative hematoma. In contrast to smoking cessation evidence, evidence regarding alcohol interventions in preventing postoperative infections is less conclusive.<sup>43,44</sup>

### MRSA Colonization

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a particularly difficult bacterium to eradicate in PJI. As the mean cost of treating a single case of MRSA-related prosthetic infection is \$107,264 vs \$68,053 for susceptible strains,<sup>45,46</sup> many infection-containment strategies focus on addressing benign MRSA colonization before surgery.

MRSA is present in the nares of 25 million people in the United States. Nasal colonization increases the risk of bacteremia 4-fold<sup>47</sup> and SSI 2- to 9-fold.<sup>48,49</sup> Nasal swabs are analyzed with either a rapid polymerase chain reaction (PCR) test, which provides results in 2 hours, or a bacterial culture, which provides results in 1 to 4 days. The PCR test is more expensive.

Eradication of MRSA colonization is increasingly prevalent. Several Scandinavian countries have instituted strict practices by which patients are denied elective surgery until negative nasal swabs are obtained.<sup>49</sup> Nasal decontamination is one method of colonization reduction. Topical mupirocin, which yields eradication in 91% of nasal carriers immediately after treatment and in 87% after 4 weeks,<sup>50</sup> is effective in reducing SSI rates only when used in conjunction with a body wash, which is used to clean the axilla and groin.<sup>51</sup> There is no consensus on optimal timing, but Bode and colleagues<sup>52</sup> found a significant decrease in deep SSIs when decontamination occurred just 24 hours before surgery.

Povidone-iodine showers went out of favor with the realization that chlorhexidine gluconate acts longer on the skin surface.<sup>53,54</sup> Preoperative showers involve rinsing with liquid chlorhexidine soap 24 to 48 hours before surgery. However, chlorhexidine binds preferentially to the cotton in washcloths instead of the skin. Edmiston and colleagues<sup>54,55</sup>

found that 4% chlorhexidine liquid soaps achieve much lower skin chlorhexidine concentrations than 2% polyester cloths do. Use of these "chlorhexidine wipes" the night before and the day of surgery has decreased PJI after TKA from 2.2% to 0.6%.<sup>56,57</sup>

## Intraoperative Risk Prevention

### Preparation

Which preoperative antibiotic to use is one of the first operative considerations in PJI prophylaxis (**Table 2**). Cefazolin is recommended as a first-line agent for its excellent soft-tissue penetration, long half-life, and activity against gram-positive bacteria such as skin flora.<sup>58</sup> Clindamycin may be considered for patients allergic to  $\beta$ -lactam antibiotics. Vancomycin may be considered for adjunctive use with cephalosporins in cases of known MRSA colonization. Vancomycin infusion should be started earlier than infusion with other antibiotics, as vancomycin must be infused slowly and takes longer to become therapeutic.

Antibiotic dosing should be based on local antibiograms, adjusted dosing weight, or BMI.<sup>59</sup> For revision arthroplasty, preoperative prophylaxis should not be stopped out of fear of affecting operative cultures.<sup>60</sup> Some surgeons pause antibiotic use if a preoperative joint aspirate has not been obtained. Infusion within 1 hour of incision is part of the pay-for-performance guidelines established by the US Centers for Medicare & Medicaid Services.<sup>61</sup> An antibiotic should be redosed if the operation will take longer than 2 half-lives of the drug.<sup>59</sup> Surgeons should consider administering a dose every 4 hours or whenever blood loss exceeds 1000 mL.<sup>62</sup> Engesæter and colleagues<sup>63</sup> found that antibiotic prophylaxis was most effective given 4 times perioperatively (1 time before surgery, 3 times after surgery). Postoperative antibiotics should not be administered longer than 24 hours, as prolonged dosing confers no benefit.<sup>58</sup>

Operating room conditions must be optimized for prophylaxis. More people and operating room traffic in nonsterile corridors increase contamination of instruments open to air.<sup>64</sup> Laminar airflow systems are commonly used. Although there is little dispute that laminar flow decreases the bacterial load of air, there are mixed results regarding its benefit in preventing PJI.<sup>65-68</sup>

Skin preparation may address patient risk factors. Hair clipping is preferred to shaving, which may cause microabrasions and increased susceptibility to skin flora.<sup>69</sup> Patients should be prepared

**Table 2. Comprehensive Strategies for Decreasing Incidence of Periprosthetic Joint Infection**

<b>Preoperative</b>
Avoid psoriatic plaques for planned incision sites
Avoid hyperglycemia
Renal transplantation for chronic kidney disease
Treat symptomatic urinary tract infections
Continue methotrexate, corticosteroids, hydroxychloroquine, and sulfasalazine
Pause use of leflunomide, anakinra, rituximab, and tumor necrosis factor $\alpha$ inhibitors
Dietary consultation for obesity
Bariatric surgery for morbid obesity
Smoking cessation
Alcohol cessation
Topical mupirocin for methicillin-resistant <i>Staphylococcus aureus</i> (MRSA) decontamination
Chlorhexidine wipes for MRSA decontamination
<b>Intraoperative</b>
Prophylactic antibiotics within 1 hour of incision
Minimize operating room traffic
Laminar airflow systems
Hair clipping over planned incision site
Sterile skin preparation
Hand scrubbing
Body exhaust suits
Sterile draping
Double surgical gloves
Change suction tip intermittently
Minimize operating room time
Minimize blood loss and transfusions
Use antibiotic cement
Dilute povidone-iodine lavage
Skin closure with barbed monofilament suture
Skin closure with topical skin adhesive
Apply antimicrobial wound dressing
<b>Postoperative</b>
Minimize hospital stay
Avoid excessive anticoagulation
Avoid hyperglycemia
Invasive procedure (eg, dental, gastrointestinal, genitourinary) antibiotic prophylaxis

with antiseptic solution. One randomized controlled trial found that 2% chlorhexidine gluconate mixed with 70% isopropyl alcohol was superior to 10% povidone-iodine in preventing SSIs.<sup>70</sup> However, a recent cohort study showed a lower rate of superficial wound infections when 1% povidone-iodine (vs 0.5% chlorhexidine) was used with alcohol.<sup>71</sup> This finding may indicate the need for alcohol preparation, higher concentrations of chlorhexidine, or both.

Proper scrubbing and protective gear are needed to reduce surgeon risk factors. Hand washing is a routine part of any surgery. Alcohol-based hand scrubs are as effective as hand scrubbing.<sup>65</sup> They reduce local skin flora by 95% immediately and by 99% with repeated applications.<sup>72</sup> Lidwell and colleagues<sup>73</sup> found a 75% reduction in infection when body exhaust suits were used in combination with laminar flow in a multicenter randomized controlled trial of 8052 patients. Sterile draping with impermeable drapes should be done over properly prepared skin. Ioban drapes (3M) are often used as a protective barrier. Interestingly, a Cochrane review found no benefit in using plastic adhesives impregnated with iodine over sterilely prepared skin.<sup>74</sup>

### Operative Considerations

Surgical gloves become contaminated in almost one third of cases, half the time during draping.<sup>75</sup> For this reason, many surgeons change gloves after draping. In addition, double gloving prevents a breach of aseptic technique should the outer glove become perforated.<sup>76</sup> Demircay and colleagues<sup>77</sup> assessed double latex gloving in arthroplasty and found the outer and inner gloves perforated in 18.4% and 8.4% of cases, respectively. Punctures are most common along the nondominant index finger, and then the dominant thumb.<sup>77,78</sup> Perforation is more common when 2 latex gloves are worn—vs 1 latex glove plus an outer cloth

glove—and the chance of perforation increases with surgery duration. The inner glove may become punctured in up to 100% of operations that last over 3 hours.<sup>79</sup> Although Dodds and colleagues<sup>80</sup> found no change in bacterial counts on surgeons' hands or gloves after perforation, precautions are still recommended. Al-Maiyah and colleagues<sup>81</sup> went as far as to recommend glove changes at 20-minute intervals and before cementation.

Surgical instruments can be sources of contamination. Some authors change the suction tip every hour to minimize the risk of deep wound infection.<sup>82-85</sup> Others change it before femoral canal preparation and prosthesis insertion during THA.<sup>86</sup> The splash basin is frequently contaminated, and instruments placed in it should not be returned to the operative field.<sup>87</sup>

Hargrove and colleagues<sup>88</sup> suggested pulsatile lavage decreases PJI more than bulb syringe irrigation does, whereas others argued that high-pressure lavage allows bacteria to penetrate more deeply, which could lead to retention of more bacteria.<sup>89</sup> Minimizing operating room time was found by Kurtz and colleagues<sup>90</sup> and Peersman and colleagues<sup>91</sup> to decrease PJI incidence. Carroll and colleagues<sup>71</sup> correlated longer tourniquet use with a higher rate of infection after TKA; proposed mechanisms include local tissue hypoxia and lowered concentrations of prophylactic antibiotics.

Similarly, minimizing blood loss and transfusion needs is another strategy for preventing infection. Allogenic transfusion may increase the risk of PJI 2 times.<sup>23,71,92</sup> The mechanism seems to be immune system modulation by allogenic blood, which impairs microcirculation and oxygen delivery at the surgical site.<sup>23,75</sup> Transfusions should be approached with caution, and consideration given to preoperative optimization and autologous blood donation. Cherian and colleagues<sup>93</sup> reviewed different blood management strategies and found preoperative iron therapy, intravenous erythropoietin, and autologous blood donation to be equally effective in reducing the need for allogenic transfusions. Numerous studies of tranexamic acid, thrombin-based hemostatic matrix (FloSeal; Baxter Inc), and bipolar sealer with radiofrequency ablation (Aquamantys; Medtronic Inc) have found no alterations in infection rates, but most have used calculated blood loss, not PJI, as the primary endpoint.<sup>94-105</sup>

Antibiotic cement also can be used to block infection.<sup>63,106-110</sup> Although liquid gentamicin may weaken bone cement,<sup>111</sup> most antibiotics, including powdered tobramycin and vancomycin, do

not weaken its fatigue strength.<sup>111-114</sup> A recent meta-analysis by Parvizi and colleagues<sup>115</sup> revealed that deep infection rates dropped from 2.3% to 1.2% with use of antibiotic cement for primary THAs. Cummins and colleagues,<sup>116</sup> however, reported the limited cost-effectiveness of antibiotic cement in primary arthroplasty. Performing povidone-iodine lavage at the end of the case may be a more inexpensive alternative. Brown and colleagues<sup>117</sup> found that rinsing with dilute povidone-iodine (.35%) for 3 minutes significantly decreased the incidence of PJI.

Closure techniques and sutures have been a focus of much of the recent literature. Winiarsky and colleagues<sup>34</sup> advocated using a longer incision for obese patients and augmenting closure in fattier areas with vertical mattress retention sutures, which are removed after 5 days. A barbed monofilament suture (Quill; Angiotech Inc) is gaining in popularity. Laboratory research has shown that bacteria adhere less to barbed monofilament sutures than to braided sutures.<sup>118</sup> Smith and colleagues<sup>119</sup> found a statistically nonsignificant higher rate of wound complications with barbed monofilament sutures, whereas Ting and colleagues<sup>120</sup> found no difference in complications. These studies were powered to detect differences in time and cost, not postoperative complications. Skin adhesive (Dermabond; Ethicon Inc), also used in closure, may be superior to staples in avoiding superficial skin abscesses.<sup>121</sup> Although expensive, silver-impregnated dressing has antimicrobial activity that reduces PJI incidence by up to 74%.<sup>122</sup> One brand of this dressing (Aquacel; ConvaTec Inc) has a polyurethane waterproof barrier that allows it to be worn for 7 days.

Three factors commonly mentioned in PJI prevention show little supporting evidence. Drains, which are often used, may create a passage for postoperative infection and are associated with increased transfusion needs.<sup>123,124</sup> Adding antibiotics to irrigation solution<sup>125</sup> and routinely changing scalpel blades<sup>126-129</sup> also have little supporting evidence. In 2014, the utility of changing scalpel blades after incision was studied by Lee and colleagues,<sup>130</sup> who reported persistence of *Propionibacterium acnes* in the dermal layer after skin preparation. Their study, however, was isolated to the upper back region, not the hip or knee.

### Postoperative Risk Prevention

Most arthroplasty patients receive anticoagulation after surgery, but it must be used with caution.

Large hematomas can predispose to wound complications. Parvizi and colleagues<sup>131</sup> associated wound drainage, hematoma, and subsequent PJI with an INR above 1.5 in the early postoperative period. Therefore, balanced anticoagulation is crucial. Postoperative glucose control is also essential, particularly for patients with diabetes. Although preoperative blood glucose levels may or may not affect PJI risk,<sup>15,17,132</sup> postoperative blood glucose levels of 126 mg/dL or higher are strongly associated with joint infections.<sup>133</sup> Even nondiabetic patients with postoperative morning levels over 140 mg/dL are 3 times more likely to develop an infection.<sup>17</sup>

Efforts should be made to discharge patients as soon as it is safe to do so. With longer hospital stays, patients are more exposed to nosocomial organisms and increased antibiotic resistance.<sup>5,23,134</sup> Outpatient antibiotics should be considered for dental, gastrointestinal, and genitourinary procedures. Oral antibiotic prophylaxis is controversial, as there is some evidence that dental procedures increase the risk of PJI only minimally.<sup>10,135-138</sup>

## Conclusion

PJI is a potentially devastating complication of TJA. For this reason, much research has been devoted to proper diagnosis and treatment. Although the literature on PJI prophylaxis is abundant, there is relatively little consensus on appropriate PJI precautions. Preoperative considerations should include medical comorbidities, use of immunocompromising medications, obesity, nutritional factors, smoking, alcohol use, and MRSA colonization. Surgeons must have a consistent intraoperative method of antibiotic administration, skin preparation, scrubbing, draping, gloving, instrument exchange, blood loss management, cementing, and closure. In addition, monitoring of postoperative anticoagulation and blood glucose management is important. Having a thorough understanding of PJI risk factors may help reduce the incidence of this devastating complication.

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*This paper will be judged for the Resident Writer's Award.*