

# RESEARCH

# Reducing surgical site infection in arthroplasty of the lower limb

A MULTI-DISCIPLINARY APPROACH

# **Objectives**

To review the current best surgical practice and detail a multi-disciplinary approach that could further reduce joint replacement infection.

# **Methods**

Review of relevant literature indexed in PubMed.

# Results

Surgical site infection is a major complication following arthroplasty. Despite its rarity in contemporary orthopaedic practice, it remains difficult to treat and is costly in terms of both patient morbidity and long-term health care resources.

# Conclusions

Emphasis on education of patients and all members of the health-care team and raising awareness in how to participate in preventative efforts is imperative.

Keywords: Surgical site infection, Hip, Knee arthroplasty, Prevention, Multidisciplinary approach

# **Article focus**

- This article reviews the evidence for methods of reducing surgical site infection in joint replacement
- We describe a multidisciplinary approach to prevent surgical site infection

# **Key messages**

- Surgical site infection in arthroplasty is potentially a devastating complication
- There are many factors that contribute to cause surgical site infections
- A multidisciplinary approach can reduce infection rates

# **Strengths and limitations**

Strengths: this review of the current literature provides the reader with a concise summary of evidence-based advice with which to make an informed decision on how to best prevent surgical site infections in lower limb arthroplasty using a multidisciplinary approach

Limitations: there are gaps in knowledge that require further research

# Introduction

Joint replacement is safe and cost effective.<sup>1</sup> Prosthetic infection is a major, but infrequent, complication with a risk of between 0.54% and 0.63% in England.<sup>2</sup> Revision of infected implants is associated with substantial morbidity and economic cost.<sup>3-5</sup> Surgical site infection (SSI) is multifactorial, involving patient, surgical and environmental factors. This paper reviews the current best surgical practice and describes how a multi-disciplinary approach can reduce peri-operative joint infection.

# **Surgical site infection**

SSI is present when pathogenic organisms multiply in a wound causing local signs and symptoms, and eventually a systemic inflammatory response. Figure 1 shows the common pathogenic organisms responsible for orthopaedic SSIs.<sup>6</sup> Infection rates increase with a greater number of patient or surgery specific risk factors<sup>7,8</sup> (Table I).

# **Modifiable patient risk factors**

Patient-related factors, such as diabetes mellitus (DM) and rheumatoid arthritis (RA), are

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Bar chart showing the distribution of micro-organisms reported as causing surgical site infections (SSIs) in mandatory orthopaedic categories, England, 2011/12 (MSSA, methicillin-sensitive *Staphylococcus aureus*; MRSA, methicillin-resistant *S. aureus*; -ve, negative; 'Other bacteria', mostly comprising isolates reported as 'unspecified diphtheroids', *corynebacterium* spp. and 'other gram-positive organisms'). Adapted with permission from the Health Protection Agency.<sup>6</sup>

modifiable and certain aspects of management can be optimised to reduce infection.

**Diabetes mellitus.** Wound infection has been shown to be more common in patients with diabetes after arthroplasty, and in non-diabetic patients who developed transient post-operative hyperglycaemia.<sup>9</sup> Hyperglycaemia is associated with increased monocyte susceptibility to apoptosis<sup>10</sup> and impaired neutrophil function (impaired chemotactic, phagocytic and bactericidal capability).<sup>11</sup> Blood glucose levels > 11.1 mmol/l are associated with SSIs in cardiac surgery,<sup>12</sup> and in general surgical patients, immediate post-operative hyperglycaemia is associated with SSI.<sup>13</sup> The potential to improve *in vivo* neutrophil phagocytic function by aggressive glucose control (using infusion delivery) has also been demonstrated in cardio-pulmonary bypass patients.<sup>14</sup>

**Rheumatoid arthritis.** RA is an independent risk factor for infection in arthroplasty, but also for revision and subsequent re-infection; pertinent given that these patients often present earlier for arthroplasty.

Local and systemic corticosteroids have been shown to delay wound-healing, increase the risk of wound infection and cause adrenal insufficiency.<sup>15</sup> A recent Cochrane review has questioned the historical practice of providing long-term users with additional peri-operative steroids (which may amplify immunosuppression at time of surgery).<sup>16</sup>

Although disease-modifying anti-rheumatic drugs (DMARDs) increase the risk of prosthetic joint infection,<sup>8</sup> the British Society for Rheumatology (BSR) guidelines suggest that in most cases these should not be stopped before joint replacement.<sup>17</sup> Methotrexate is a commonly used first-line drug<sup>18</sup> and, despite its inclusion within the DMARD group, is not considered to increase wound infection risk, and should not be discontinued before orthopaedic surgery.<sup>19</sup> However, nitrous oxide should be excluded from the anaesthetic regimen as the interaction can induce immuno-suppression.<sup>20</sup>

Tumour necrosis factor (TNF)- $\alpha$  is an inflammatory cytokine (highly concentrated in the synovial tissue of RA patients) implicated in joint destruction.<sup>21</sup> Any increase in risk of infection in patients who received anti-TNF therapy before surgery is debatable.<sup>22,23</sup> The BSR state that the potential benefit of preventing post-operative infections (by stopping treatment) should be balanced against the risk of a peri-operative disease flare. If anti-TNF therapy is to be withheld, it should be discontinued between five and 20 days before surgery (three to five times the half-life of the drug), restarting when there is good wound healing and no evidence of infection.<sup>24</sup>

**Obesity.** The effect of obesity on SSI, defined as a body mass index (BMI)  $\geq$  30 kg/m<sup>2</sup>,<sup>25</sup> is well documented.<sup>26</sup> In a prospective study of over 2800 knee and hip replacements, Namba et al<sup>27</sup> found that the odds ratio was between 4.2 and 6.7 times the risk for infection in obese total knee and hip patients, respectively, compared with non-obese patients. Increased length and complexity of surgery, and poorer vascularisation of the subcutaneous layer may contribute to this elevated

Table I. Methods for reducing surgical site infection in joint replacement

Risk factor	Summary <sup>*</sup>
Patient factors	
Diabetes mellitus	Aggressive glucose control
Rheumatoid arthritis	DMARDs and methotrexate should not be stopped Peri-operative steroids are generally not required Balance the risks and benefits of stopping anti-TNF – stop at 3 to 5 half-lives pre-operative, restart after wound healing and no evidence of infection Nitrous oxide should be avoided in patients on methotrexate
Obesity	Dietician input to encourage weight loss Adjust peri-operative antibiotic doses appropriately In extremely obese consider bariatric surgery before surgery
Smoking	Consider a smoking cessation programme
Carrier screening	MRSA and MSSA screening based on local guidelines, and decolonise before admission
<b>Pre-operative factors</b> Patient preparation	Shower on day of surgery If shaving required, use electric clippers on day of surgery Avoid oil-based skin moisturisers
Antibiotics	Prophylactic antibiotics should be given as early as possible in the anaesthetic room, and continued for 24 hours post-oper- atively (antibiotic type dependent on local guidelines) Administer antibiotics at least 5 minutes before tourniquet inflation If cementation is required, antibiotic-impregnated should be used
Peri-operative factors	
Theatre	Use laminar flow where possible Keep theatre door opening to a minimum
Personnel	Hand wash with antiseptic surgical solution, using a single-use brush or pick for the nails Before subsequent operations hands should be washed with either an alcoholic hand rub or an antiseptic surgical solution Double glove and change gloves regularly Polyprophylene non-woven gowns with adequate mask and hat coverage
Skin preparation	Use an alcohol pre-wash followed by a 2% chlorhexadine-alcohol scrub solution
Anaesthetic	Maintain normothermia Maintain normovolaemia A higher inspired oxygen concentration peri-operatively and for 6 hours post-operative may be of benefit
Drapes	Use of iodine-impregnated incise drapes may be of benefit (in patients without allergy)
Blood transfusion	Optimise pre-operative haemoglobin If possible, transfusion should be avoided intra-operatively and if anticipated should be given more than 48 hours before surgery Antifibrinolytics may indirectly reduce SSI by reducing the need for transfusion
Post-operative factors	
Dental procedures	Insufficient evidence to recommend the use of prophylactic antibiotics for patients undergoing routine dental procedures following joint replacement

\* DMARDs, disease-modifying anti-rheumatic drugs; TNF, tumour necrosis factor; MRSA, methicillin-resistant Staphylococcus aureus; MSSA, methicillin-sensitive S. aureus; SSI, surgical site infection

risk. Obese patients also require a significantly higher fraction of inspired oxygen (FIO<sub>2</sub>) to reach an adequate arterial oxygen level.<sup>28</sup> Referral to a dietician may be necessary. In extremely obese patients ( $\geq$  50 kg/m<sup>2</sup>), bariatric surgery may be indicated. In patients undergoing both bariatric surgery and lower limb arthroplasty, the rate of wound infection was 3.5 times lower in patients who had bariatric surgery first.<sup>29</sup> Communication with the anaesthetist is recommended in order to evaluate the risk and to discuss increased doses of peri-operative antibiotics.<sup>30</sup> **Smoking.** Smoking is associated with impaired wound healing and infection.<sup>31</sup> Patients randomised to a cessation programme six to eight weeks before arthroplasty surgery had significantly fewer wound complications (5% *versus* 31%), shorter length of stay, fewer reoperations and non-quantified cardiovascular benefits compared with those who had continued smoking.<sup>32</sup> **Screening and decolonisation.** The costs associated with treatment of infections due to methicillin-resistant organ

isms are 1.5 times higher compared with sensitive organisms.<sup>33</sup> A methicillin-resistant *Staphylococcus aureus* 

(MRSA) screening programme for all planned NHS surgery was implemented in April 2009,<sup>34</sup> with a positive result prompting decolonisation before admission.

Nasal carriers of methicillin-sensitive *S. aureus* (MSSA) also have an increased risk of infection. In a large, randomised multicentre trial, the risk of developing hospital-associated *S. aureus* infection in MSSA-carrier patients who were decolonised on admission to hospital (mupirocin nasal ointment and chlorhexidine soap) fell by nearly 60% compared with placebo – a significant reduction from 7.7% to 3.4%.<sup>35</sup> Nasal carriage of MSSA is common (approximately 20%<sup>35</sup>), and United Kingdom hospitals are beginning to decolonise patient carriers before joint replacement.

### **Pre-operative phase surgical risk factors**

**Patient preparation before theatre.** Patients should shower with soap on the morning of surgery.<sup>36</sup> Washing with an antiseptic reduces skin bacteria (microflora), but there is little evidence of a reduction in risk of SSI.<sup>37,38</sup> Dry shaving with a razor may irritate the skin and increase the bacterial count, so if hair removal is necessary, electric clippers or depilatory creams on the day of surgery are favoured.<sup>36,39</sup> **Type of antibiotic prophylaxis.** The role of parenteral prophylactic antibiotics has been studied and accepted across most surgical specialties,<sup>40,41</sup> and may be the single most important factor in the prevention of deep wound infection following lower limb arthroplasty.<sup>42</sup>

Although many different groups of antibiotics can be used for prophylaxis, there is insufficient evidence of a significant difference in the efficacy of cephalosporins, teicoplanin or penicillin-derivatives, or a benefit of one generation of cephalosporins over another.<sup>43</sup> Cephalosporin use has been associated with *Clostridium difficile* colitis, especially in the elderly, but rates are low after joint replacement (1.7 per 1000 replacements).<sup>44</sup>

Aminoglycosides, such as gentamicin, can be administered locally (in the cement) or parenterally. In a review of 15 000 primary total hip replacements from the Norwegian Arthroplasty Register, the lowest risk of revision was found in patients who received both systemic and local (in cement) antibiotics.<sup>45</sup>

**Timing of antibiotic prophylaxis.** The United Kingdom National Institute of Health and Clinical Excellence (NICE) recommends a single intravenous dose of antibiotic prophylaxis on starting anaesthesia, with a repeat dose if the operation is longer than the half-life of the antibiotic, or if blood loss is a significant.<sup>46,47</sup> The American Academy of Orthopaedic Surgeons (AAOS) state that the administration of antibiotic should precede the skin incision by one hour, and duration of prophylaxis should not exceed 24 hours.<sup>48</sup> Rates of infection have been found to be lowest for patients who received an antibiotic within two hours of the incision,<sup>40</sup> and there was no difference between one-and three-day courses of prophylactic antibiotics in terms of deep-infection rate.<sup>49</sup> It would seem prudent to give antibiotics as early as possible in the anaesthetic room, well

before (at least 5 minutes) tourniquet inflation limits any further rise in tissue antibiotic concentration.<sup>50</sup>

### Peri-operative phase surgical risk factors

**Theatre etiquette.** The World Health Organization recommends that all surgical staff should keep doors to the operating room closed, except as needed for the passage of equipment, personnel and the patient.<sup>51</sup> Staff should store essential equipment in the operating room to decrease theatre traffic.<sup>51</sup> Frequency of theatre door-opening is a positive predictor of raised bacterial counts.<sup>52</sup>

Alcohol rub used in preparation for surgery may be as effective as hand scrubbing in preventing SSIs.<sup>53</sup> There is no evidence to suggest that any particular alcohol rub is better than another.<sup>54,55</sup>

**Surgical site preparation in theatre.** Skin moisturisers appear to inhibit the ability of aqueous preparations to decolonise the skin, and may increase skin bacteria counts. Avoidance of oil based moisturisers and de-greasing with alcohol pre-wash is recommended.<sup>56</sup>

A randomised trial of 849 patients undergoing cleancontaminated surgery in which pre-operative skin preparation was performed with either 2% chlorhexidine-alcohol or aqueous povidone-iodine and paint found that the rate of SSI was significantly lower in the chlorhexidinealcohol group.<sup>57</sup>

Theatre design. Airborne contaminants are the largest single contributor to infection.<sup>58</sup> One billion skin cells are shed daily per person,<sup>59</sup> with up to 10% carrying bacteria.<sup>60</sup> For orthopaedic surgery, laminar-flow ventilation systems have been advocated,<sup>61</sup> although they are not in universal use. These employ high-efficiency particulate air filters where particles larger than 0.3 µm are removed (5 µm for conventional theatres). Ultra-clean air has reduced bacterial and particle concentrations.<sup>62</sup> Ultraclean air and prophylactic antibiotics have independent and additive effects on reducing infections after joint arthroplasty.<sup>63</sup> There is no dispute that the air within an effective laminar flow theatre is extremely clean. However, Brandt et al<sup>64</sup> found laminar flow to have no protective effect against SSI in 99 230 patients. When 88 311 arthroplasty patients from the New Zealand joint registry were analysed, revision rates for deep infection were significantly higher in laminar flow theatres, despite adjustment for other known variables.<sup>65</sup> As a result of these findings, the authors questioned the routine use of laminar air flow in arthroplasty, feeling that the added expense to the health service was not justified.<sup>65</sup> Before abandoning laminar flow, the interaction with forced air warming should be examined. A recent study demonstrated that air from outside the canopy may be drawn into the surgical wound area when forced air warming (FAW) devices are used, and deep infection rates were reduced when FAW was abandoned in favour of contemporary conductive fabric warming in joint replacement.<sup>66</sup>

Operating personnel clothing. NICE recommends double gloving in arthroplasty surgery.<sup>46,67</sup> Glove perforation increases the risk of transmission of blood-borne diseases and breaks the asepsis barrier, potentially allowing contamination of the wound and thus increasing the risk of infection.<sup>68,69</sup> Studies have shown that use of a blunt needle compared with a sharp needle during surgery reduces glove perforation rates significantly.<sup>70,71</sup> Most perforations are unnoticed (61.5%) and are caused by shearing rather than penetration by sharps.<sup>68</sup> A Cochrane systematic review supported the use of double gloving, despite no evidence of a reduction in SSI.<sup>72</sup> Glove changing at regular intervals is an effective way to decrease the length of exposure to bacterial contamination during total hip replacement.<sup>69</sup> Latex-free gloves have significantly higher perforation rates when compared with latex gloves.<sup>73</sup>

Hooper et al,<sup>65</sup> in their ten-year New Zealand joint registry study, found that the rate of revision for early deep infection had not been reduced by space suits compared with a normal theatre gown and mask, when analysed independently of laminar flow.

**Surgical drapes.** NICE recommend an incise drape impregnated with iodophore should be used unless the patient has an iodine allergy.<sup>46</sup> Although a Cochrane review concluded that these drapes did not make any difference to infection rates,<sup>74</sup> only one trial involved orthopaedic surgery, which showed no difference in post-operative wound infection rates following hip fracture surgery with or without non-impregnated Opsite (Smith & Nephew Wound Management, Hull, United Kingdom).<sup>75</sup>

**Body core temperature.** Peri-operative hypothermia is common during major surgery and causes vasoconstriction, resulting in a reduction in subcutaneous tissue perfusion and an increased risk of infection.<sup>76</sup> Peri-operative hypothermia is associated with increased blood loss, cardiac events, increased transfusion requirements and longer perioperative hospital stay.<sup>77</sup> Heat loss in theatre is largely conductive and convective, with a small amount of radiated heat. Laminar flow significantly increases convective heat loss in exposed patients, mitigated by active warming.

Warming patients undergoing clean general surgery significantly reduces wound infection.<sup>78</sup> A similar report of cholecystectomy patients found nearly a six-fold difference in the incidence of wound infection between normothermic and hypothermic patients.<sup>79</sup> The importance of maintaining peri-operative normothermia has been recognised in the recent NICE guidelines.<sup>80</sup> However, it is notable that warming has never been proven to reduce SSIs in orthopaedic implant surgery, and their effect on laminar flow and clean air needs further study.

**Oxygen delivery and fluid management.** Increasing tissue oxygen concentrations has been hypothesised to increase the killing potential of phagocytes and thus decrease infective complications in the peri-operative period.<sup>81</sup> Enhancement of tissue oxygen delivery can be

achieved via improvement of cardiac output and/or oxygen content of the blood. Increased subcutaneous oxygen concentrations can be achieved by increasing the inspired oxygen concentration intra-operatively (from 30% to 80%), and by providing supplemental oxygen post-operatively. There are studies supporting the use of supplemental oxygen to reduce wound infections in general surgery, but these have never been extrapolated to arthroplasty surgery.<sup>82-84</sup>

Both hypovolaemia and hypervolaemia (oedema) can be detrimental to tissue oxygenation. Current guidance would support optimal tissue oxygenation by maintenance of a normovolaemic state throughout the peri- and early post-operative period by judicious use of intravenous fluids.<sup>85,86</sup>

Anaesthetic technique. The question of whether regional anaesthesia is superior to general anaesthesia has yet to be adequately assessed, although a recent retrospective population based study found a significantly lower 30-day rate of SSI in patients undergoing lower limb arthroplasty under a spinal anaesthetic compared with patients undergoing similar procedures under general anaesthetic.<sup>87</sup> An RCT examining the potentially beneficial effect of nitrous oxide avoidance failed to show a reduction in SSI. Co-administered anaesthetic and sedative agents may impair immune responses directly, thereby increasing infection,<sup>88</sup> and regional anaesthesia may offer particular benefits such as improved tissue oxygen delivery (through vasodilation). Randomised controlled trials are required to address whether choice of agent (such as use of an alpha-2 adrenergic versus GAB-Aergic sedative) affects outcome.<sup>88,89</sup>

**Anaemia.** In a prospective cohort study pre-operative anaemia was associated with increased post-operative infections in patients undergoing hip arthroplasty.<sup>90</sup> This effect was associated with an increase in post-operative blood transfusion.

Blood transfusion. There are no specific recommendations from NICE regarding transfusions. Though it is clear that blood loss is primarily a surgical responsibility, regional anaesthetic techniques and attention to perioperative normothermia are associated with reduced blood loss. Transfusion related immunomodulation is recognised in trauma patients<sup>91</sup> with a 5% increase risk of infection for every unit of red cells given.<sup>92</sup> A significant increase in infection rates following hip replacement are seen in patients receiving allogeneic red blood cells, with higher risk with more units transfused.<sup>93</sup> There is clearly a risk-benefit balance between immunosuppression and enhancing oxygen supply to hypoperfused tissue. If possible, blood transfusion should be avoided intra-operatively94 and, if anticipated, should be administered at least 48 hours before surgery to maximise oxygen transportation of transfused blood. Addressing pre-operative anaemia reduces postoperative transfusion requirements.

The use of antifibrinolytics, such as tranexamic acid, prevent blood loss following major arthroplasty.<sup>95</sup> Although there is insufficient data to comment on their ability to prevent post-operative infection, they may indirectly reduce the risk by reducing transfusion requirement and improving the wound environment.

### **Post-operative period**

**Thromboembolic prophylaxis.** NICE guidelines state that patients undergoing lower limb joint replacements should have either prophylactic low-molecular-weight heparin (LMWH) or an orally active direct factor Xa inhibitor for 28 (or 35) days following hip replacement and 14 days following a knee replacement.<sup>96</sup> No increased risk of infection was found with LMWH<sup>97</sup> but prolonged ooze is a recognised risk,<sup>98</sup> and each day of prolonged wound drainage increases risk of wound infection by between 29% and 42% following arthroplasty.<sup>98</sup> Wound related complications following arthroplasty may increase in patients who receive a factor Xa inhibitor for thromboprophylaxis.<sup>99</sup>

**Dental care and other procedures.** It has been suggested that patients requiring dental care post-arthroplasty should receive prophylactic antibiotics.<sup>100</sup> Other authors argue that there is little evidence to suggest that bacteraemia associated with dental procedures causes prosthetic joint infection<sup>101</sup>; simple tasks, such as brushing teeth and chewing, can produce a greater bacteraemia than one dental procedure and it would be better practice for the surgeon to ensure dentition and oral health are up to standard before elective orthopaedic surgery. Currently in the United Kingdom, the British Dental Association does not recommend antibiotics in patients undergoing dental procedures and who are at risk of infective endocarditis.<sup>102</sup>

### Conclusions

SSI following routine surgery can have disastrous consequences for the patients and causes a significant drain on the resources of healthcare providers. A multidisciplinary approach is essential in order to reduce infection rates. Every possible step must be exercised to reduce contamination of the surgical wound and to optimise the patient's capacity to eradicate any colony forming units entering the wound. Common sense approaches are required to minimise or correct physiological disturbances and attention should be given to theatre design and etiquette, identification and control of MSSA carriers and the appropriate and timely use of prophylactic antibiotics. It is important to emphasise the need to educate the patient and all members of the health-care team, and to increase awareness of the importance of their participation in preventive efforts.

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