Prevention of infection in primary THA and TKA

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Rates of peri-prosthetic joint infection (PJI) in primary total hip and total knee arthroplasty range between 0.3% and 1.9%, and up to 10% in revision cases. Significant morbidity is associated with this devastating complication, the economic burden on our healthcare system is considerable, and the personal cost to the affected patient is immeasurable.

The risk of surgical site infection (SSI) and PJI is related to surgical factors and patient factors such as age, body mass index (BMI), co-morbidities, and lifestyle. Reducing the risk of SSI in primary hip and knee arthroplasty requires a multi-faceted strategy including pre-operative patient bacterial decolonization, screening and avoidance of anaemia, peri-operative patient warming, skin antisepsis, povidone-iodine wound lavage, and anti-bacterial coated sutures.

This article also considers newer concepts such as the influence of bearing surfaces on infection risk, as well as current controversies such as the potential effects of blood transfusion, laminar flow, and protective hoods and suits, on infection risk.

Keywords: arthroplasty; hip; infection; knee; surgical site infection (SSI)

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Introduction

The publication of Joseph Lister’s ‘Antiseptic principle in the practice of surgery’ in 1867 revolutionized surgical practice.1 Despite his critics at the time, the routine use of antiseptic skin preparation for everything from venepuncture to major surgery became universally accepted as a method for reducing infection rates. The development of antibiotics and their use in surgical prophylaxis in many branches of surgical practice has also become commonplace, and has further reduced infection. Despite the ongoing evolution and refinement of surgical practice, surgical site infection (SSI) remains a risk for every patient, including those undergoing primary total hip and knee arthroplasty procedures, and is associated with a three-fold mortality rate at one year. The overall incidence of SSI following primary total hip arthroplasty (THA) is between 0.2% and 2.2%2 and rates of deep or peri-prosthetic joint infection (PJI) in THA and primary total knee arthroplasty (TKA) range between 0.3% and 1.9%,3 and up to 10% in revision cases.4 The risk of SSI and PJI is related to surgical factors and patient factors such as age, body mass index (BMI), co-morbidities, and lifestyle.5 Significant morbidity is associated with this devastating complication, the economic burden on our healthcare system is considerable, and the personal cost to the affected patient is immeasurable.6–8 This article is not an exhaustive list on infection prevention, but will discuss more recent tactics in modern orthopaedic practice to reduce infection rates in primary THA and TKA surgery.

Patient warming

Patient exposure in the operating theatre combined with the vasodilatory effects of anaesthetic agents and the continuous air changes associated with the use of ultra-clean laminar airflow, cause a progressive fall in core temperature, placing patients at risk of peri-operative hypothermia, defined as a core temperature less than 36°C. Other actions such as pre-washing patients and infusion of cool fluids serve to exacerbate the effects. Reductions in core temperature of 2°C are associated with a three-fold risk of SSI, thought to be related to impaired soft tissue oxygen delivery caused by peripheral vasoconstriction, a physiological response to the fall in core temperature,9 and reduced collagen deposition, leading to impaired wound healing.10 In addition, an attenuated stress and immune response caused by lower core temperature is thought to contribute to the increased rate of SSI.11,12 Up to 66% of patients experience peri-operative hypothermia and the risk is clearly increased in patients undergoing longer procedures.13–17 Intra-operative warming has become established as a standard of care in many countries but pre-warming is not. However, NICE guidance18 recommends that active warming should start at least 30 minutes before induction of anaesthesia in all patients, unless this will delay emergency surgery, and that induction of
anaesthesia should be delayed unless the patient’s body temperature is greater than 36°C. The guidance also goes on to say that active warming should continue throughout the operative phase, and that if the patient’s body temperature falls below 36°C at any point during the 24-hour post-operative period, active warming should be re-instated. Intra-operative patient temperature falls even in those who have warming devices applied to the skin, and evidence has shown that this decrease in core temperature can be offset along with the associated risk of complications such as infection, by warming patients pre-operatively for 30 minutes. In addition, core body temperature has been shown to fall twice as much in patients who are not warmed prior to transfer to the operating theatre. Other benefits of avoiding hypothermia aside from reduced infection rates include reduced hospital stay, reduced blood loss, and reduced mortality.

Forced air warming (FAW) devices have traditionally been the most widely used type of patient warming devices in orthopaedic surgery, and studies in colorectal, breast, vascular and hernia surgery have shown them to reduce infection rates. However, there is concern that forced air warming devices which expel air at approximately 20°C warmer than the ambient temperature in theatre, cause a significant temperature gradient and associated convection currents, which could interfere with the effectiveness of laminar air flow. Ascending warm air flow currents can, in theory, impede the downward current of laminar air flow, with reductions in the latter having been shown to increase the entry of contaminants to the surgical wound. An alternative to forced air warming devices are conductive fabric arming devices which are more thermally efficient, thereby releasing less heat into the immediate environment, and they have been shown to be just as effective at reducing peri-operative hypothermia. The 2018 Philadelphia international consensus on the prevention of PFIs reiterated that ‘there is no evidence to definitively link FAW to an increased risk of SSIs/PFIs. Alternative methods of warming can be effective and may be used’. Trials are needed comparing infection rates with forced air warming and resistive fabric warming devices and a pilot study has been completed.

Laminar flow

It has long been acknowledged that air flow within the operating theatre has a role in infection prevention, related to the transfer of airborne particles colonized with bacteria to the surgical wound, and that operating in ultraclean air can reduce the rate of SSI significantly, as demonstrated in Lidwell’s work, which included a multi-centre randomized controlled trial (RCT) incorporating over 8000 arthroplasty patients. Ultraclean ventilation within theatres subsequently became the gold standard within orthopaedic operating theatres, and works to protect open wounds from airborne contaminants by providing a constant, uniform flow of high velocity (0.3–0.5 m/s), highly filtered air, which results in more than 500 air changes per hour, and a reduction in bacterial colony forming units (CFUs) from 5.4/ft² to 0.45/ft². This is aided by the passage of air through a high efficiency particulate air (HEPA) filter, which removes 99.97% of all particles that are > 0.3 μm in size. However, since laminar flow was initially heralded as one of the most important advances in infection control, it has fallen from grace to some degree, with several sources questioning its effectiveness at reducing infection rates. Laminar air flow is not currently recommended by the World Health Organization for reducing the risk of infection when carrying out arthroplasty surgery. However, the effectiveness of laminar flow is dependent on its air flow currents being able to act unhindered, and it may well be that other measures routinely employed to reduce infection rates are impacting on laminar air flow’s effectiveness. As mentioned previously, convection currents, particularly related to forced air warming, have been shown to interfere with laminar air flow currents. In addition, the position of satellite operating theatre lights over surgical wounds, and the movement of theatre staff under the laminar flow canopy has been shown to be detrimental to the effectiveness of laminar air flow, causing an increase in CFUs. Those using laminar flow theatres should take precautions to ensure theatre lights are not positioned directly above the surgical wound to avoid disruption to the downward flow. Instrument trolleys, once open, should remain strictly within the laminar flow canopy, as even at a point 10 cm beyond its boundary, the air is contaminated with around 3 million particles per square metre. Theatre traffic and movement of personnel should be restricted to an absolute minimum.

Space suits

Protective suits and hoods were introduced to the orthopaedic operating theatre in an effort to further reduce the rate of infection in conjunction with already established laminar flow. People are known to shed around 10⁷ skin cells per day and up to 10% of these carry bacteria. The movement of theatre personnel within the immediate vicinity of the surgical wound creates disturbances in air currents and produces airborne contaminants such as skin and hair particles, primarily shed by healthcare workers. The original total body exhaust suits introduced by Charnley were designed to eliminate this significant factor in an effort to further reduce infection rates. These suits used negative pressure to draw exhaust gases out of the suit to an area outside of the canopy. Early rates of arthroplasty infection were as high as 9.5%, but by 1982, a large RCT showed a reduction in infection rates of 90% related to the
use of total body exhaust suits, ultraclean air and prophylactic antibiotics. However, exhaust tubing was eventually abandoned and modern protective suits were produced for personal protection of clinical teams. These differ in that air produced by the fan within the helmet and the expiratory gases of the wearer create positive pressure within the suit, pushing potentially contaminated air out through gaps in the suit, such as those around the neck, sleeves and back, directly into the laminar flow canopy, in close proximity to the surgical wound. Concerns have arisen about the use of these suits, with several studies, including one from the New Zealand Joint Registry, showing that they are associated with significantly increased infection rates. This is a contentious issue, as many surgeons are likely to feel these suits provide vital personal protection. There is a heightened awareness of blood-borne viruses and the potential risk that patients pose to surgeons, especially in an environment where high-speed power tools convert patient body fluids, bone and cement into aerosols and high-speed projectiles. Some of the concerns about potentially contaminated air escaping from modern space suits can be mitigated by taping sleeves around the inner glove to prevent air escape from sleeves. We would advocate further studies to establish the benefits and risks with respect to infection prevention and modern space suits.

**Blood transfusion**

Hip and knee arthroplasty is associated with a level of blood loss that on occasion necessitates blood transfusion, although rates of blood transfusion vary widely between arthroplasty units, from 2% to 70%. Contributed to by the fact that there is no universally accepted guidelines in place for the use of blood transfusion in arthroplasty surgery. The transfusion rate in arthroplasty has dropped dramatically in recent years with the prevalent use of tranexamic acid, with oral formulations showing significant cost benefit and reduced transfusion rates when compared with intravenous use. The rate of mortality rises exponentially with falling haemoglobin levels, but blood transfusion carries risks of acute transfusion reactions, haemolysis, transfusion-related acute lung injury, graft vs. host disease, and transfusion-transmitted infections. In addition, data are accumulating to suggest that allogenic blood transfusion may be an infection risk to patients following joint arthroplasty, thought to be related to immunosuppressive effects, which include attenuated IL-2 production, inhibition of natural killer cell activity and a decreased delayed-type hypersensitivity response. Other studies have shown that immunosuppressive leukocytes within allogenic blood are responsible for some of these immunomodulatory changes. A large meta-analysis of over 21,000 THA and TKA patients showed a significantly higher rate of SSI in patients who were given allogenic blood transfusions (2.88% vs. 1.74%). A more recent retrospective case control study involving more than 27,000 patients undergoing primary THA and TKA demonstrated an overall incidence of blood transfusion of 11.1%, which was associated with a significantly increased risk of superficial infection (adjusted odds ratio [OR] 1.9 [95% CI 1.2–2.9, p-value 0.005]) as well as deep infection (adjusted OR 1.6 [95% CI 1.1–2.2, p-value 0.008]). A study involving 2760 patients undergoing primary hip and knee arthroplasty procedures in Germany, showed that the overall complication rate in patients who received transfusions was 34.7% compared with 13.2% in patients who did not require transfusion, with infection rates of 2.82% and 0.4% respectively.

The length of time that blood products have been stored prior to transfusion has been shown to have an effect on infection rates. Structural and functional changes, or ‘storage lesions’ occur within red blood cells when they are stored for prolonged periods. This includes alterations in cell membrane expression of the marker CD47 and phosphatidylserine, and release of cytokines, histamine and other immunologically active substrates such as potassium, damaged and oxidized proteins and lipids into the supernatant. Several studies have found an increased rate of infection with prolonged red blood cell storage (> 14 days) in cardiac surgery patients who have received transfusions. A more recent study analysing infection rates in 199 patients following blood transfusion in abdominal, orthopaedic, vascular and urological surgery, found that there was a higher rate of wound infection in patients receiving blood aged > 14 days vs. patients receiving blood aged < 14 days (relative risk [RR] 3.1). The study also showed a significantly increased incidence of acute kidney injury in patients who were recipients of older blood. One theory for the increased risk of infection following blood transfusion relates to the effects of iron. One unit of red blood cells (RBCs) contains 220–250 mg of iron, and following transfusion, engulfment of non-viable RBCs by the monocyte/macrophage system can affect cytokine release and exacerbate or cause a systemic inflammatory response. Increased circulating iron, especially non-transferrin-bound iron, is also associated with prolonged storage of red blood cells, and can increase proliferation of particular pathogens such as *Staphylococcus aureus*.

The risks of blood transfusion are clearly best avoided with a strategy of prevention, with a comprehensive anaemia screening programme in which iron and haemoglobin levels are assessed pre-operatively, with efforts made to correct deficiencies pre-operatively, and involvement of a multi-disciplinary team incorporating haematologists and general practitioners when appropriate. This has been shown to significantly reduce transfusion rates, length of stay, re-admission rate, and critical care admissions.
Surgical site antisepsis

Pathogens responsible for SSI are predominantly from skin, and skin antisepsis is therefore a vital step in infection prevention. The most commonly used formulations for skin antisepsis worldwide include aqueous and alcoholic forms of povidone-iodine and chlorhexidine-based solutions. A large 2010 meta-analysis of seven RCTs involving almost 3500 patients, compared chlorhexidine at various concentrations (0.5–4.0%) with povidone-iodine (7–10%) for skin preparation in clean and contaminated surgery, and found that chlorhexidine was associated with fewer SSIs (RR 0.64; 95% CI 0.51–0.80). Another meta-analysis of six RCTs comparing chlorhexidine (0.5–4.0%) with povidone-iodine (7.5–10.0%) demonstrated similar findings (pooled OR 0.68, 95% CI 0.50–0.94). However, in both of these meta-analyses, studies which used alcoholic and non-alcoholic-based preparations were compared, which makes interpretation difficult. A single-centre randomized controlled trial recruited 1147 obstetric patients and compared the use of 2% chlorhexidine –70% isopropanol and 8.3% povidone-iodine –70% isopropanol, and found a 4.0% vs. 7.3% rate of SSI respectively (RR 0.55; 95% CI 0.34–0.90). Similarly, a comparison of 2% chlorhexidine –70% isopropanol and 5% povidone-iodine –70% alcohol for the insertion of vascular catheters in 2546 patients showed a lower rate of infection with chlorhexidine-based solutions (hazard ratio 0.15, 95% CI 0.05–0.41; p = 0.0002).81

Povidone-iodine lavage of wounds prior to closure is an important strategy in minimizing infection risk in THA and TKA. Betadine contains povidone-iodine which is inhibitory to biofilm production by organisms such as Staphylococcus epidermidis and Staphylococcus aureus. It has a broad spectrum of activity, including against methicillin-resistant S. aureus. Several studies have found beta-lavage of wounds prior to closure to reduced infection rates significantly. A three-minute lavage with 3.5% povidone-iodine of primary THA and TKA wounds prior to closure, in a study of 1862 cases, found that the infection rate fell from 0.97% to 0.15%. A similar protocol was applied to patients undergoing spinal surgery; in 208 patients who underwent povidone-iodine lavage, no superficial or deep infections occurred. However, when povidone-iodine lavage was not used, the rate of deep infection was 2.9%, and superficial 0.5%. A recently published RCT studying the effects of three-minute povidone-iodine lavage vs. normal saline lavage on infection rates, in revision surgery for aseptic THA and TKA, showed a significantly reduced infection rate at 90 days with the use of povidone-iodine (3.4% vs. 0.4%, p = .038).

Suture material

Sutures may be integral to infection risk. Even modern sutures are not inert materials, and induce a local inflammatory response. Sutures also serve as a surface on which bacteria can potentially coalesce, and some materials may be more amenable to the formation of biofilms than others. Bacterial adherence to braided sutures has been shown to be five to eight times higher than adherence to monofilament such as nylon. In the same way that an established biofilm on a joint prosthesis makes bacterial eradication difficult, the same applies to sutures, leading to an increased risk of SSI. An animal model of S. aureus infection into which prosthetic heart valve sewing rings were implanted subcutaneously, showed that coating the implants with a combination of minocycline and rifampicin reduced the rate of colonization, compared to implants coated with silver coated and uncoated prostheses. The antibacterial properties of triclosan (polychlorophenoxyphenol)-coated sutures have been of interest in recent years after gaining approval for this use in the USA in 2002, with multiple in vivo and in vitro studies showing a beneficial effect in reducing SSI, including an animal study in 2007 which demonstrated a 66% reduction in Staphylococcus epidermidis SSI. The senior author conducted a two-arm, parallel, double-blinded study involving 2546 patients undergoing elective total hip (THA) and total knee arthroplasty (TKA) at three hospitals within our institution, comparing standard sutures and triclosan-coated sutures. We established an infection rate of 0.8% in the control group and 0.7% in the intervention group, although our findings did not reach statistical significance. More recently, we performed a meta-analysis incorporating 25 RCTs and 11,957 patients showed that triclosan-coated sutures significantly reduced the rate of SSI at 30 days (RR 0.73, 95% CI 0.65–0.82). Ten RCTs within this meta-analysis were focused on clean surgery, for which a significantly lower incidence of SSI (149/3029) occurred with triclosan-coated sutures compared to standard sutures (230/1117) (RR 0.71, 95% CI 0.58–0.88). We estimate that the prevention of one SSI saves around £2000 in joint replacement costs – and as such is highly cost-effective.

Ongoing debate surrounds the issue of skin closure and whether sutures or clips are superior for reducing SSI, or if it makes any difference at all. There are very few published RCTs on the subject, and those that have been published contain relatively few patient numbers from which to draw reasonable comparisons. A recent meta-analysis was performed which analysed 17 RCTs with a total of 2446 patients comparing sutures and clips for skin closure in orthopaedic surgical procedures. This showed no difference in SSI risk when staples were used instead of sutures for skin closure. However, within this study, only 5/15
RCTs including 501 patients in total were deemed to be of low bias, and when these were analysed no difference was found in incidence of SSI between the two groups. When the authors considered RCTs involving elective THA and TKA (seven studies and 967 patients), again no significant difference was found.92

MSSA decolonization

One third of patients are colonized with methicillin-sensitive S. aureus (MSSA), and this reservoir serves as the source of infection in more than 80% of healthcare-associated S. aureus infections.93 Healthy subjects are rarely carriers of S. aureus: 60% are intermittent carriers and 20% are persistent carriers. Carriage of the bacteria is most commonly within the nasal passages,94 but it is also a prevalent skin commensals. The incidence of nosocomial S. aureus bacteraemia has been shown to be three times higher in S. aureus carriers than in non-carriers,95 and colonized patients are also at increased risk of SSI, as well as having an increased mortality rate.96 Skin decontamination with chlorhexidine has long been known to be an effective method of reducing staphylococcal colony counts.97 Bode et al performed a large multi-centre RCT, in which they used real-time polymerase chain reaction (PCR) to assess whether patients were carriers of S. aureus. They established that all of the S. aureus strains identified were susceptible to mupirocin and randomized patients to receive placebo treatment or eradication therapy with 2% mupirocin nasal ointment and chlorhexidine gluconate soap for skin. In the intervention and placebo groups respectively, 87.5% and 88.9% of patients underwent surgical procedures. Decolonization treatment reduced the risk of superficial and deep S. aureus SSI (RR 0.45, 95% CI 0.18–1.11 and RR 0.21 95% CI 0.07–0.62 respectively), and was also associated with shorter length of hospital stay.93 The study demonstrated an overall 60% reduction in S. aureus-associated infections in patients who received eradication therapy. A meta-analysis published prior to this considered the effect of mupirocin on surgical patients colonized with S. aureus and also demonstrated a significant benefit, with a reduction of 45% in hospital-associated S. aureus infection.98 In our unit, we screen patients routinely and administer decolonization therapy when appropriate, with mupirocin nasal ointment in conjunction with octenidine wash for skin decontamination. A study of 12,910 primary arthroplasties (5917 hip, 6993 knee) performed in our unit showed that PJI MSSA rate was 0.75% under.109 A study of the New Zealand Joint Registry reviewed 97,889 who underwent primary THAs over a 15-year period.110 No relationship was found with the rate of early PJI (< six months), but CoC hips were associated with a significantly lower risk of revision for deep infection when compared with metal-on-polyethylene (MoP) over the whole study period of 15 years. However, the authors recommend caution in interpretation of these results due to a lack of data on American Society of Anaesthesiologists class (ASA) and BMI. Analysis of the Emilia-Romagna region Registry for Orthopaedic Prosthetic Implants (RIPO), incorporating 39,206 patients with a mean age of 68 years, who underwent primary cementless THA, showed that CoC bearing surfaces had a significantly lower rate of PJI compared to MoM, during the study period of 13 years, although this difference was not apparent during the first six months following surgery.117 A United States study of 315,784 Medicare patients over the age of 65 years who underwent primary THA between 2005 and 2014, showed

Bearing surfaces

Evidence is accumulating that the bearing surfaces used in THA may be of great importance in terms of subsequent risk of PJI. Ceramic bearings have been shown to have lower wear rates in comparison to cobalt-chrome and polyethylene associated with lower levels of osteolysis.100–102 Evidence from joint registries suggests that ceramic-on-ceramic (CoC) bearing surfaces may be associated with lower levels of infection compared with more commonly used metal-on-polyethylene (MoP) articulations.108–110 An analysis of 623,253 patients who underwent primary hip procedures from the National Joint Registry of England and Wales, has shown that CoC and ceramic-on-polyethylene (CoP) bearing surfaces are associated with a reduced risk of revision for PJI compared with MoP (RR 0.6 and 0.7 respectively at two years or longer post surgery).108 This finding may be related to observations in vitro which demonstrate reduced bacterial adhesion on ceramic arthroplasty surfaces,111,112 with significantly lower numbers of colony forming units (CFUs) present on biofilms in ceramic (230 CFU/ml) compared with polyethylene (6250 CFU/ml) and metal bearings (5870 CFU/ml).112 In vitro and in vivo work has also shown less bacterial biofilm formation on ceramic bearing surfaces when compared with metal and polyethylene.113–116 There are other clinical studies to support these findings, such as an analysis of the Australian registry (AOANJRR) incorporating 177,237 patients who underwent primary THA. Ceramic-on-ceramic bearing surfaces were shown to have lower revision rates for infection when compared with metal-on-highly cross-linked polyethylene and ceramic-on-highly cross-linked polyethylene bearings, in patients aged 70 years and under.109 A study of the New Zealand Joint Registry reviewed 97,889 who underwent primary THAs over a 15-year period.110 No relationship was found with the rate of early PJI (< six months), but CoC hips were associated with a significantly lower risk of revision for deep infection when compared with CoC, MoP, and metal-on-metal (MoM) over the whole study period of 15 years. However, the authors recommend caution in interpretation of these results due to a lack of data on American Society of Anaesthesiologists class (ASA) and BMI. Analysis of the Emilia-Romagna region Registry for Orthopaedic Prosthetic Implants (RIPO), incorporating 39,206 patients with a mean age of 68 years, who underwent primary cementless THA, showed that CoC bearing surfaces had a significantly lower rate of PJI compared to MoM, during the study period of 13 years, although this difference was not apparent during the first six months following surgery.117 A United States study of 315,784 Medicare patients over the age of 65 years who underwent primary THA between 2005 and 2014, showed
significantly reduced risk of infection when CoP or CoC bearings were used, compared with MoP bearings.\textsuperscript{118}

Although no bearing surface currently in use for THA can negate the risk of infection, the evidence for ceramic bearing surfaces in reducing risk of PJI is persuasive. However, the cost of ceramic implants remains high and we would advocate further large-scale analysis of registry data and cost-benefit analysis to determine whether wider-scale use of ceramic surfaces is warranted.

**Conclusions**

The numbers of patients undergoing THA and TKA continues to increase with an ever-ageing population. Infection following primary arthroplasty occurs infrequently but is a devastating complication with significant morbidity, mortality and massive costs to healthcare economies, affecting huge numbers of patients worldwide. Infection prevention in arthroplasty requires a multi-faceted approach. We have discussed relevant factors including patient bacterial decolonization, avoidance of anaemia, blood transfusion, peri-operative patient warming, laminar flow, space suits, careful skin antisepsis, povidone-iodine wound lavage, triclosan-coated sutures, and bearing surfaces.

There are questions about modern protective hoods and suits due to the positive pressure expulsion of air from around the wearer’s skin, out into the immediate vicinity of surgical wounds. Data from New Zealand in relation to this equipment and the increased rates of infection associated with it are of particular concern.\textsuperscript{37} However, many arthroplasty surgeons will be reluctant to stop wearing protective hoods, due to flying debris and bodily fluids in theatre and the personal risk associated with this. Viable alternatives need to be sought, perhaps with a reversion back to total body exhaust suits such as those originally introduced by Charnley, which were known to reduce infection risk.\textsuperscript{49}

Preventing anaemia is a vital step in reducing infection risk. We consider a comprehensive, multi-disciplinary pre-operative anaemia screening programme is of paramount importance in optimizing patients for surgery. Anaemia should be recognized and treated well in advance of surgery, to avoid the associated risks of exacerbating pre-existing anaemia which include cardiac ischaemia, impaired wound healing and increased risk of requiring blood transfusion. Blood transfusion poses many risks of its own, including risk to life. The literature also demonstrates an increased risk of infection associated with blood transfusion, particularly or perhaps exclusively when patients are recipients of blood aged more than 14 days.\textsuperscript{72} However, although blood is usually readily available, the luxury of being able to request blood that is less than 14 days old is not. NICE has published guidance on thresholds for blood transfusion and target haemoglobin, although blood transfusion rates following arthroplasty continue to vary.\textsuperscript{53}

The pathogens responsible for most SSI come from the patient’s own skin,\textsuperscript{93} and measures to reduce or eradicate skin commensals at the surgical site must be taken. Povidone-iodine has been used traditionally for many years, but evidence seems to be clear that alcohol-based chlorhexidine is superior for skin antisepsis, and is recommended as the first-line skin antisepsis agent by NICE.\textsuperscript{78,79}

 MSSA decolonization must be performed to reduce patient pathogen load. It is clear that patients who carry MSSA are at increased risk of infection, no matter how meticulous local skin preparation is around the surgical site, and eradication is an important step to minimize risk. All patients should be screened pre-operatively and provided with chlorhexidine skin wash and mupirocin nasal drops where appropriate.\textsuperscript{93}

Research regarding triclosan-coated sutures is of interest. Although our own work looking at infection rates with this type of suture showed no benefit compared with standard sutures, a large meta-analysis shows a definite benefit of triclosan sutures,\textsuperscript{91} and although more expensive, there is an overall cost saving in relation to a reduced infection rate.\textsuperscript{119} We have not yet incorporated triclosan-coated sutures into our practice but plan to do so, based on this evidence.

We have observed the accumulating evidence relating to ceramic bearing surfaces, and the associated reduced risk of PJI, with interest. There is evidence to suggest reduced bacterial adhesion to ceramic molecules and reduced biofilm formation when compared with other bearing surfaces, and registry data from multiple sources show that this is associated with lower rates of failure secondary to PJI. Lower levels of osteolysis observed with ceramic bearings may also suggest a reduced inflammatory response to ceramic particles. We advocate implementation of further large-scale analysis of registry data, RCTs and cost-benefit analyses.

In summary, there is no single intervention that will abolish infection risk for arthroplasty patients. Clearly some patients are more susceptible than others to infection, but even the healthiest are at risk. Based on current evidence, arthroplasty surgeons should employ multiple tactics in their practice to reduce the risk of SSI, although controversy exists as to what constitutes best practice.

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REFERENCES
1. Lister J. On the antiseptic principle in the practice of surgery. Br Med J. 1867;2:246–248.
2. Namba RS, Inacio MC, Paxton EW. Risk factors associated with surgical site infection in 30,491 primary total hip replacements. J Bone Joint Surg Br. 2012;94:1330–1338.
3. Brown NM, Cipriano CA, Moric M, Sporer SM, Della Valle CJ. Dilute betadine lavage before closure for the prevention of acute postoperative deep periprosthetic joint infection. J Arthroplasty 2012;27:27–30.
4. Negus JJ, Gifford PB, Haddad FS. Single-stage revision arthroplasty for infection: an underutilized treatment strategy. J Arthroplasty 2017;32:2053–2055.
5. Diener MK, Knebel P, Kieser M, et al. Effectiveness of triclosan-coated PDS Plus versus uncoated PDS II sutures for prevention of surgical site infection after abdominal wall closure: the randomised controlled PROUD trial. Lancet 2014;384:142–152.
6. Drehorn CR, Hamblen DL. Revision arthroplasty: a high price to pay. BMJ 1989;298:648–649.
7. Haddad FS, Ngu A, Negus JJ. Prosthetic joint infections and cost analysis? Adv Exp Med Biol 2017;971:93–100.
8. Cahill JL, Shadbolt B, Scarvell JM, Smith PN. Quality of life after infection in total joint replacement. J Orthop Surg (Hong Kong) 2008;16:58–65.
9. Kurz A, Sessler DI, Lenhardt R; Study of Wound Infection and Temperature Group. Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. N Engl J Med 1996;334:1209–1215.
10. Prockop DJ, Kirivirikko KJ, Tuderman L, Guzman NA. The biosynthesis of collagen and its disorders (first of two parts). N Engl J Med 1979;301:13–23.
11. Melling AC, Ali B, Scott EM, Leaper DJ. Effects of preoperative warming on the incidence of wound infection after clean surgery: a randomised controlled trial. Lancet 2000;355:876–880.
12. Schäffer M, Barbul A. Lymphocyte function in wound healing and following injury. Br J Surg 1998;85:444–460.
13. Vaughan MS, Vaughan RW, Cork RC. Postoperative hypothermia in adults: relationship of age, anesthesia, and shivering to rewarming. Anesth Analg 1981;60:746–751.
14. Karalapillai D, Story D, Hart GK, et al. Postoperative hypothermia and patient outcomes after major elective non-cardiac surgery. Anaesthesia 2013;68:605–611.
15. Abelha FJ, Castro MA, Neves AM, Landeiro NM, Santos CC. Hypothermia in a surgical intensive care unit. BMC Anesthesiology 2005;5:7.
16. Leijtens B, Koëter M, Kremers K, Koëter S. High incidence of postoperative hypothermia in total knee and total hip arthroplasty: a prospective observational study. J Arthroplasty 2013;28:895–898.
17. Karalapillai D, Story D, Hart GK, et al. Postoperative hypothermia and patient outcomes after elective cardiac surgery. Anaesthesia 2011;66:780–784.
18. National Institute for Health and Care Excellence (2008). Hypothermia: prevention and management in adults having surgery. Updated December 2016. from: https://www.nice.org.uk/guidance/cg66/ (date last accessed 26 March 2020).
19. Just B, Trévien V, Delva E, Lienhart A. Prevention of intraoperative hypothermia by preoperative skin-surface warming. Anesthesiology 1993;79:214–218.
20. Schmied H, Kurz A, Sessler DI, Kozek S, Reiter A. Mild hypothermia increases blood loss and transfusion requirements during total hip arthroplasty. Lancet 1996;347:289–292.
21. Bush HL Jr, Hydo LJ, Fischer E, Fantini GA, Silane MF, Barie PS. Hypothermia during elective abdominal aortic aneurysm repair: the high price of avoidable morbidity. J Vasc Surg 1995;21:392–400.
22. Mahoney CB, Odom J. Maintaining intraoperative normothermia: a meta-analysis of outcomes with costs. AANA J 1999;67:155–163.
23. McGovern PD, Albrecht M, Belani KG, et al. Forced-air warming and ultra-clean ventilation do not mix: an investigation of theatre ventilation, patient warming and joint replacement infection in orthopaedics. J Bone Joint Surg Br 2011;93:1532–1544.
24. Chow TT, Yang XY. Ventilation performance in the operating theatre against airborne infection: numerical study on an ultra-clean system. J Hosp Infect 2005;59:138–147.
25. Ng V, Lai A, Ho V. Comparison of forced-air warming and electric heating pad for maintenance of body temperature during total knee replacement. Anaesthesia 2006;61:1000–1004.
26. Kimberger O, Held C, Stadelmann K, et al. Resistive polymer versus forced-air warming: comparable heat transfer and core rewarming rates in volunteers. Anesth Analg 2008;107:1621–1626.
27. International consensus meeting on prosthetic joint infection 2018. Does the use of forced air warming (FAW) during orthopaedic procedures increase the risk of subsequent surgical site infections/periprosthetic joint infections (SSIs/PJIs)? 2018. https://icmphilly.org.uk/guidance/cg65/ (date last accessed 26 March 2020).
28. Kümin M, Deery J, Turney S, et al. Reducing Implant Infection in Orthopaedics (RIIiO): results of a pilot study comparing the influence of forced air and resistive fabric warming technologies on postoperative infections following orthopaedic implant surgery. J Hosp Infect 2019;103:412–419.
29. Lidwell OM, Lowbury EJL, Whyte W, Blowers R, Stanley SJ, Lowe D. Airborne contamination of wounds in joint replacement operations: the relationship to sepsis rates. J Hosp Infect 1983;4:111–131.
30. Lidwell OM. Clean air at operation and subsequent sepsis in the joint. Clin Orthop Relat Res 1986;211:91–102.
31. Lidwell OM, Elson RA, Lowbury EJ, et al. Ultraclean air and antibiotics for prevention of postoperative infection: a multicenter study of 8,052 joint replacement operations. Acta Orthop Scand 1987;58:4–13.
32. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for prevention of surgical site infection, 1999. Centers for Disease Control and Prevention (CDC)
Hospital Infection Control Practices Advisory Committee. *Am J Infect Control* 1995;23:79–132; quiz 3–4; discussion 96.

33. Nelson JP, Glassburn AR Jr, Talbott RD, McElhinney JP. The effect of previous surgery, operating room environment, and preventive antibiotics on postoperative infection following total hip arthroplasty. *Clin Orthop Relat Res* 1980;147:167–169.

34. Singh S, Reddy S, Shrivastava R. Does laminar airflow make a difference to the infection rates for lower limb arthroplasty: a study using the National Joint Registry and local surgical site infection data for two hospitals with and without laminar airflow. *Eur J Orthop Surg Traumatol* 2017;27:261–265.

35. Bischoff P, Kubilay NZ, Allegranzi B, Egger M, Gastmeier P. Effect of laminar airflow ventilation on surgical site infections: a systematic review and meta-analysis. *Lancet Infect Dis* 2017;17:553–561.

36. Jain S, Reed M. Laminar air flow handling systems in the operating room. *Surg Infect (Larchmt)* 2019;20:151–158.

37. Hooper GJ, Rothwell AG, Frampton C, Wyatt MC. Does the use of laminar flow (Larchmt) 2019;20:151–158.

38. Brandt C, Hott U, Sohr D, Daschner F, Gastmeier P, Rüden H. Surgical site infection data for two hospitals with and without laminar airflow. *Eur J Orthop Surg Traumatol* 2017;27:261–265.

39. Bischoff P, Kubilay NZ, Allegranzi B, Egger M, Gastmeier P. Effect of laminar airflow ventilation on surgical site infections: a systematic review and meta-analysis. *Lancet Infect Dis* 2017;17:553–561.

40. Dasari KB, Albrecht M, Harper M. Effect of forced-air warming on the performance of operating theatre laminar airflow ventilation. *Anaesthesia* 2013;67:244–249.

41. Refaie R, Rushton P, McGovern P, et al. The effect of operating lights on laminar airflow: an experimental study using neutrally buoyant helium bubbles. *Bone J Joint* 2017;99-B:1061–1066.

42. Hubble MJ, Weale AE, Pever JY, Bowker KE, MacGowan AP, Bannister GC. Clothing in laminar-flow operating theatres. *J Hosp Infect* 1996;32:1–7.

43. Whyte W. The role of clothing and drapes in the operating room. *J Hosp Infect* 1988;11 Suppl C:2–17.

44. Noble WC. Dispersal of skin microorganisms. *Br J Dermatol* 1975;93:477–485.

45. Whyte W, Hodgson R, Tinkler J. The importance of airborne bacterial contamination of wounds. *J Hosp Infect* 1982;3:123–135.

46. Nelson JP. Five years experience with operating room clean rooms and personnel-isolator systems. *Med Instrum* 1976;10:277–281.

47. Feagin JA Jr. Bacteriology of the operating room with the use of helmet aspiration systems. *Arch Surg* 1979;114:790–792.

48. Charnley J. The classic. A clean-air operating enclosure. By John Charnley. 1964. *Clin Orthop Relat Res* 1986;211:4–9.

49. Lidwell OM, Lowbury EJ, Whyte W, Blowers R, Stanley SJ, Lowe D. Effect of ultraclean air in operating rooms on deep sepsis in the joint after total hip or knee replacement: a randomised study. *Br Med J (Clin Res Ed)* 1982;285:10–14.

50. Young SW, Zhu M, Shirley OC, Wu Q, Spangehl MJ. Do ‘surgical helmet systems’ or ‘body exhaust suits’ affect contamination and deep infection rates in arthroplasty? A systematic review. *J Arthroplasty* 2016;31:225–233.

51. Vijaysegaran P, Knibbs LD, Morawska L, Crawford RW. Surgical space suits increase particle and microbiological emission rates in a simulated operating environment. *J Arthroplasty* 2018;33:1524–1529.

52. Young SW, Chisholm C, Zhu M. Intraoperative contamination and space suits: a potential mechanism. *Eur J Orthop Surg Traumatol* 2014;24:409–413.

53. Friedman R, Homering M, Holberg G, Berkowitz SD. Allogeneic blood transfusions and postoperative infections after total hip or knee arthroplasty. *J Bone Joint Surg Am* 2014;96:272–278.

54. Spahn DR. Anaemia and patient blood management in hip and knee surgery: a systematic review of the literature. *Anaesthesiology* 2010;113:482–495.

55. Irwin A, Khan SK, Jameson SS, Tate RC, Copeland C, Reed, MR. Oral versus intravenous tranexamic acid in enhanced-recovery primary total hip and knee replacement. *Bone J Joint* 2013;95-B:1556–1561.

56. Shander A, Javidroozi M, Ozawa S, Hare GMT. What is really dangerous: anaemia or transfusion? *Br J Anaesth* 2011;107:141–159.

57. Youssef LA, Spitalnik SL. Transfusion-related immunomodulation: a reappraisal. *Curr Opin Hematol* 2017;24:551–557.

58. Blumberg N, Heal JM. Transfusion and recipient immune function. *Arch Pathol Lab Med* 1989;113:246–253.

59. Bordin JO, Heddle NM, Blajchman MA. Biologic effects of leukocytes present in transfused cellular blood products. *Blood* 1994;84:1703–1721.

60. Blajchman MA. Transfusion immunomodulation or TRIM: what does it mean clinically? *Hematology* 2005;10:208–214.

61. Wood ML, Gottschalk R, Monaco AP. Effect of blood transfusion on IL-2 production. *Transplantation* 1988;45:930–935.

62. Jensen LS, Andersen AJ, Christiansen PM, et al. Postoperative infection and natural killer cell function following blood transfusion in patients undergoing elective colorectal surgery. *Br J Surg* 1992;79:553–561.

63. Nielsen HJ, Hammer JM, Moesaard F, Kehlet H. Comparison of the effects of SAG-M and whole-blood transfusions on postoperative suppression of delayed hypersensitivity. *Can J Surg* 1997;40:146–150.

64. Bilgin YM, van de Watering LM, Eijisman L, et al. Double-blind, randomized controlled trial on the effect of leukocyte-depleted erythrocyte transfusions in cardiac valve surgery. *Circulation* 2004;109:2755–2760.

65. Tartt PJ, Mohandas K, Azar P, Endres J, Kaplan J, Spivack M. Randomized trial comparing packed red cell blood transfusion with and without leukocyte depletion for gastrointestinal surgery. *Am J Surg* 1998;176:462–466.

66. Kim JL, Park J-H, Han S-B, Cho IY, Jang K-M. Allogeneic blood transfusion is a significant risk factor for surgical-site infection following total hip and knee arthroplasty: a meta-analysis. *J Arthroplasty* 2017;32:310–315.

67. Taneja A, El-Bakoury A, Khong H, et al. Association between allogeneic blood transfusion and wound infection after total hip or knee arthroplasty: a retrospective case-control study. *Bone J Joint* 2019;4:99–105.

68. Klasan A, Dworschak P, Heyse TJ, et al. Transfusions increase complications and infections after hip and knee arthroplasty: an analysis of 2760 cases. *Technol Health Care* 2018;26:825–832.

69. Sparror RL. Red blood cell storage and transfusion-related immunomodulation. *Blood Transfus* 2010;8 Suppl 3:s26–s30.

70. Koch CG, Li L, Sessler DI, et al. Duration of red-cell storage and complications after cardiac surgery. N Engl J Med 2008;358:1229–1239.

71. Andreassen JF, Dethlefsen C, Modrau IS, et al; North-West Denmark Transfusion Study Group. Storage time of allogeneic red blood cells is associated with uninfected red blood cell storage, but not with cellulitis.
risk of severe postoperative infection after coronary artery bypass grafting. Eur J Cardiothor Surg 2011;39:329–334.
72. Spadaro S, Taccone FS, Fogagnolo A, et al. The effects of storage of red blood cells on the development of postoperative infections after noncardiac surgery. Transfusion 2017;57:2727–2737.
73. Ozment CP, Turi JL. Iron overload following red blood cell transfusion and its impact on disease severity. Biochem Biophys Acta 2009;1790:694–701.
74. Wang L, Johnson EE, Shi HH, Walker WA, Wessling-Resnick M, Cherayil BJ. Attenuated inflammatory responses in hemochromatosis reveal a role for iron in the regulation of macrophage cytokine translation. J Immunol 2008;181:2723–2731.
75. Hod EA, Zhang N, Sokol SA, et al. Transfusion of red blood cells after prolonged storage produces harmful effects that are mediated by iron and inflammation. Blood 2010;115:4284–4292.
76. Barton Pai A, Pai MP, Depczynski J, McQuade CR, Mercier RC. Non-transferrin-bound iron is associated with enhanced Staphylococcus aureus growth in hemodialysis patients receiving intravenous iron sucrose. Am J Nephrol 2006;26:304–309.
77. Pujol-Nicolas A, Morrison R, Casson C, et al. Preoperative screening and intervention for mild anemia with low iron stores in elective hip and knee arthroplasty. Transfusion 2017;57:3049–3057.
78. Lee I, Agarwal RK, Lee BY, Fishman NO, Umscheid CA. Third-generation ceramic-on-ceramic cementless total hip arthroplasty: a minimum 10-year follow-up study. J Arthroplasty 2018;33:133–138.
80. Tuuli MG, Liu J, Stout MJ, et al. A randomized trial comparing skin antisep tic agents at Cesarean delivery. N Engl J Med 2016;374:647–655.
81. Mimoz O, Lucet J-C, Kerforne T, et al; CLEAN trial investigators. Skin antisepsis with chlorhexidine–alcohol versus povidone–iodine in clean-contaminated surgery. Br J Surg 2010;97:1614–1620.
82. Goldenheim PD. In vitro efficacy of povidone-iodine solution and cream against methicillin-resistant Staphylococcus aureus. Postgrad Med 1993;99:562–565.
83. Reimer K, Wichelhaus TA, Schäfer V, et al. Antimicrobial effectiveness of povidone-iodine and consequences for new application areas. Dermatology 2002;204:114–120.
84. Calkins TE, Culvern C, Nam D, et al. Dilute betadine lavage reduces the risk of acute postoperative perigastrointestinal joint infection in aseptic revision total knee and hip arthroplasty: a randomized controlled trial. J Arthroplasty 2020;35:538–543.e1.
85. Cristina AG, Price JL, Hobgood CD, Webb LX, Costerton JW. Bacterial colonization of percutaneous sutures. Surgery 1989;98:32–19.
86. Katz S, Izhari M, Mirelman D. Bacterial adherence to surgical sutures: a possible factor in suture induced infection. Ann Surg 1981;194:35–41.
87. Kathju S, Nistico L, Tower I, Lasko LA, Stoodley P. Bacterial biofilms on implanted suture material are a cause of surgical site infection. Surg Infect (Larchmt) 2014;15:592–600.
88. Darouiche RO, Meade R, Mansouri M, Raad II. In vivo efficacy of antimicrobial-coated fabric from prosthetic heart valve sewing rings. J Heart Valve Dis 1998;7:639–646.
106. Nikolaou VS, Edwards MR, Bogoch E, Schemitsch EH, Waddell JP. A prospective randomised controlled trial comparing three alternative bearing surfaces in primary total hip replacement. J Bone Joint Surg Br 2012;94:459–465.

107. Rodriguez JA, Cooper HJ. Large ceramic femoral heads: what problems do they solve? Bone Joint J 2013;95-B:63–66.

108. Lenguerrand E, Whitehouse MR, Beswick AD, et al. Risk factors associated with revision for prosthetic joint infection after hip replacement: a prospective observational cohort study. Lancet Infect Dis 2018;18:1004–1014.

109. Madanat R, Laaksonen I, Graves SE, Lorimer M, Muratoglu O, Malchau H. Ceramic bearings for total hip arthroplasty are associated with a reduced risk of revision for infection. Hip Int 2018;28:222–226.

110. Pitto RP, Sedel L. Periprosthetic joint infection in hip arthroplasty: is there an association between infection and bearing surface type? Clin Orthop Relat Res 2016;474:2213–2218.

111. Sorrentino R, Cochis A, Azzimonti B, et al. Reduced bacterial adhesion on ceramics used for arthroplasty applications. J Eur Ceram Soc 2018;38:963–970.

112. Trampuz A, Maiolo EM, Winkler T, Perka C. Biofilm formation on ceramic, metal and polyethylene bearing components from hip joint replacement systems. Bone Joint J - Orthop Proc 1998;98-B:80–88.

113. Pilz M, Staats K, Tobudic S, et al. Zirconium nitride coating reduced Staphylococcus epidermidis biofilm formation on orthopaedic implant surfaces: an in vitro study. Clin Orthop Relat Res 2019;477:461–466.

114. Clauss M, Furustrand Tafin U, Betrisey B, et al. Influence of physico-chemical material characteristics on staphylococcal biofilm formation: a qualitative and quantitative in vitro analysis of five different calcium phosphate bone grafts. Eur Cell Mater 2014;28:9–49, discussion 50.

115. Lass R, Giurea A, Kubista B, et al. Bacterial adherence to different components of total hip prosthesis in patients with prosthetic joint infection. Int Orthop 2014;38:1597–1602.

116. Porporati AA, Spriano S, Ferraris S, Rimondini L, Cochis A. Ceramic materials show reduced bacteria biofilm formation, because of their surface chemico-physical properties. Bone Joint J - Orthop Proc 1998;98-B:150.

117. Bordini B, Stea S, Castagnini F, Busanelli L, Giardina F, Toni A. The influence of bearing surfaces on periprosthetic hip infections: analysis of thirty nine thousand, two hundred and six cementless total hip arthroplasties. Int Orthop 2019;43:103–109.

118. Kurtz SM, Lau E, Baykal D, Springer BD. Outcomes of ceramic bearings after primary total hip arthroplasty in the Medicare population. J Arthroplasty 2017;32:743–749.

119. Leaper DJ, Edmiston CE Jr, Holy CE. Meta-analysis of the potential economic impact following introduction of absorbable antimicrobial sutures. Br J Surg 2017;104:E134–E144.