



Surgery

UNIVERSITY OF TORONTO

Surgical Site Infection Prevention

A Clinical Practice Guideline developed by the
University of Toronto's Best Practice in Surgery in collaboration
with the Antimicrobial Stewardship Program

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Section 1. General information

Aim

The aim of this guideline is to make recommendations for interventions which decrease the risk of surgical site infections in surgical patients.

Outcomes of interest

The outcomes of interest are the timely administration of appropriate antibiotics, maintenance of perioperative normothermia, and decreased surgical site infections enhanced patient recovery and increased patient satisfaction.

Target population

Adult and pediatric patients undergoing elective surgery

Intended users

This guideline is intended for use by surgeons, surgical residents and fellows, anesthesiologists, pharmacists, and nurses caring for surgical patients.

Scope

The scope of this review includes recommendations for antibiotic prophylaxis, maintenance of normothermia, skin preparation, hair removal, decolonization of *Staphylococcal aureus* carriers, and use of antibiotic impregnated cement in joint replacement.

Oral decontamination with antiseptics, glycaemia control and perioperative oxygenation with high fraction of inspired oxygen (FiO₂) of 60% to 90% were reviewed, but formal recommendations were not made because of the limited available evidence (oral decontamination with antiseptics such as chlorhexidine mouthwashes), feasibility and potential harms (oxygenation with high FiO₂) and conflicting data on efficacy (oxygenation with high FiO₂).

Rationale

Surgical site infections (SSIs) are the most common and expensive healthcare-associated infections.^{5,6} Furthermore, these infections are associated with significant morbidity (7 to 11 additional hospital-days) and mortality (2 to 11 times higher risk of death).⁷ However, evidence-based initiatives can prevent more than 50% of SSIs.⁸ While institutional guidelines are important to promote such best practices, the effectiveness of these recommendations depends on their implementation.

This guideline expands on the Best Practice in General Surgery guideline updated in 2012. It is meant to be more comprehensive and include recommendations for other surgical services. The evidence and rationale for these recommendations are also summarized.

Overview of process

This guideline was developed through primary literature review and with consideration of the WHO 2016 Global Guidelines for the Prevention of Surgical Site Infection¹, American Society of Health-System Pharmacists (ASHP) recommendations², National Institute for Health and Care Excellence (NICE) guidelines³ and Canadian Patient Safety Institute (CPSI) Surgical Site Infection: Getting Started Kit⁴. The recommendations were tailored for practice at the University of Toronto affiliated hospitals as part of the Best Practice in Surgery initiative in collaboration with the University of Toronto Antimicrobial Stewardship

Collaborative. Feedback was obtained from local experts and representatives of all Surgical Divisions. The evidence was assessed in adherence to GRADE recommendations (<http://www.gradeworkinggroup.org/>).

Section 2. Guideline recommendations

1. Antibiotic use

- 1.1 All patients having surgery should receive appropriate prophylactic antibiotics except for some clean surgical procedures (See Table 1) (Level of evidence: High)
- 1.2 Patients, who are said to have an antibiotic allergy, should have an allergy history taken to learn what antibiotic caused the reaction and clarify the type of reaction. For penicillin cross-reactions, only a history of severe/anaphylactic reactions (for example hives, hypotension, respiratory difficulties) necessitates an alternative to beta-lactams (Level of evidence: Moderate)
- 1.3 Antibiotics should be dosed to optimize tissue concentrations (See Table 2) (Level of evidence: Moderate)
- 1.4 Antibiotics should be administered within 60 minutes before surgical incision/tourniquet inflation. Vancomycin and fluoroquinolones require a longer infusion time and should be initiated to ensure completion within 60 minutes of incision (See Table 2) (Level of evidence: Low-Moderate)
- 1.5 Antibiotics should be re-dosed if the duration of the procedure exceeds two half-lives of the antibiotic (Table 1) or there is excessive blood loss (>1.5L in adults) for all antibiotics except vancomycin (Level of evidence: Very low)
- 1.6 Antibiotics should not be given postoperatively unless there is an indication other than for prophylaxis (Level of evidence: High)
- 1.7 Patients who have indwelling drains or intravascular catheters do not require additional prophylaxis (Level of evidence: Moderate)
- 1.8 In MRSA colonized patients, vancomycin should be added to the regimen (See Section 6) (Level of evidence: Moderate)
- 1.9 Patients receiving therapeutic antibiotics preoperatively are at increased risk for surgical site infections. The optimal method of prophylaxis is unknown, but unless the therapeutic antibiotic provides coverage for SSI prophylaxis, prophylactic antibiotics should be administered. As well, these antibiotics should be timed to ensure maximal tissue concentration at incision (Level of evidence: Very low)

2. Perioperative normothermia

- 2.1 Active measures should be taken to ensure that the patient's body temperature is greater than 36°C perioperatively
 - 2.1.1 If the patient is at high risk of hypothermia or if his/her temperature is less than 36°C preoperatively, forced-air warmers should be started prior to induction to ensure a body temperature greater than 36°C prior to surgery (Level of evidence: Moderate)
- 2.2 The use of forced-air warming systems (Level of evidence: Moderate) and warmed IV and irrigation fluids (Level of evidence: Very low) should be used intraoperatively to maintain body temperature greater than 36°C for patients during the surgical procedure
 - 2.2.1 Warming systems should not be used in patients undergoing surgery where intraoperative hypothermia is intended (i.e. off-pump surgery)

3. Preoperative skin preparation

- 3.1 Patients should be prepped with alcohol-based chlorhexidine gluconate (2% chlorhexidine gluconate and 70% isopropyl alcohol) with the following exceptions: (Level of evidence: Moderate)
 - 3.1.1 Povidone iodine should continue to be used for ophthalmic procedures and those involving the inner ear or mucous membranes
 - 3.1.2 Procedures where there is no time for alcohol solutions to dry (eg: in trauma), an aqueous-based antiseptic solution should be used and allowed to dry
 - 3.1.3 Infants less than 2 months old

- 3.2 Alcohol-based antiseptics are flammable in operative procedures involving electrosurgery (i.e. electrocautery) so pooling on drapes and the patient should be avoided. The antiseptic solution should also be allowed time to dry completely (~ 3 minutes, longer in areas with excess hair) to limit fire hazard (Level of evidence: Low)
- 3.3 Patients should bathe or shower the entire body and head prior to surgery using plain or antimicrobial soap

4. Preoperative hair removal

- 4.1 Hair removal should not be performed for the purposes of SSI prevention. If hair removal is necessary, clippers should be used (Level of evidence: Moderate)

5. *Staphylococcus aureus* decolonization

- 5.1 In cardiac surgery and orthopedic/spinal surgery with hardware insertion, *Staphylococcus aureus* screening with nasal swab and decolonization of carriers with intranasal mupirocin 2% ointment BID and chlorhexidine-gluconate body wash for 5 days before surgery should be considered (Level of evidence: Low)
- 5.2 For MRSA carriers, decolonization in conjunction with hospital infection control practitioners or infectious disease consultants should be considered (Level of evidence: Very low)

6. Special considerations

- 6.1 Antimicrobial-coated sutures may be used to reduce SSIs (Level of evidence: Moderate)
- 6.2 Local application of vancomycin powder in spine surgery is controversial and no strong recommendation can be made with the current evidence (Level of evidence: Very low)
- 6.3 Antibiotic impregnated shunts may be beneficial in reducing central nervous system shunt infections but no strong recommendation can be made with the current evidence (Level of evidence: Very low)
- 6.4 Endocarditis prophylaxis is only required in patients with a few predisposing cardiac conditions prior to specific dental procedures (Level of evidence: Low) and manipulation of the respiratory mucosa (Level of evidence: Very low)

Section 3. Guideline recommendations and supporting evidence

1. **Antibiotic use**
- 1.1 **All patients having surgery should receive appropriate prophylactic antibiotics except for some clean surgical procedures (See Table 1)**
- 1.2 **Patients, who are said to have an antibiotic allergy, should have an allergy history taken to learn what antibiotic caused the reaction and clarify the type of reaction. For penicillin cross-reactions, only a history of severe/anaphylactic reactions (for example hives, hypotension, respiratory difficulties) necessitates an alternative to beta-lactams**
- 1.3 **Antibiotics should be dosed to optimize tissue concentrations (See Table 2)**
- 1.4 **Antibiotics should be administered within 60 minutes before surgical incision/tourniquet inflation. Vancomycin and fluoroquinolones require a longer infusion time and should be initiated to ensure completion within 60 minutes of incision (See Table 2)**
- 1.5 **Antibiotics should be re-dosed if the duration of the procedure exceeds two half-lives of the antibiotic (Table 1) or there is excessive blood loss (>1.5L in adults) for all antibiotics except vancomycin**
- 1.6 **Antibiotics should not be given postoperatively unless there is an indication other than for prophylaxis.**
- 1.7 **Patients who have indwelling drains or intravascular catheters do not require additional prophylaxis.**
- 1.8 **In MRSA colonized patients, vancomycin should be added to the regimen (See Section 6).**
- 1.9 **Patients receiving therapeutic antibiotics preoperatively are at increased risk for surgical site infections. The optimal method of prophylaxis is unknown, but unless the therapeutic antibiotic provides coverage for SSI prophylaxis, prophylactic antibiotics should be administered. As well, these antibiotics should be timed to ensure maximal tissue concentration at incision**

There is strong evidence that prophylactic antibiotics decrease the risk of surgical site infections (SSIs). While the efficacy varies depending on the procedure and patient factors, the benefits can be dramatic. For instance, the risk of postoperative infection can be reduced by 75% for colorectal surgery using antibiotic prophylaxis⁹. The choice of antibiotic(s) varies depending on the type of procedure and the organ which is being operated on. The benefit of antimicrobial prophylaxis is less for clean surgeries and is often not required unless postoperative infections would have severe consequences such as in arthroplasties. When choosing a regimen, the narrowest antimicrobial spectrum should be used to minimize the risk of *Clostridium difficile* infections and the emergence of antibiotic resistance.

For patients at risk of Gram-negative SSIs (e.g. gastrointestinal, urological procedures), an expanded spectrum regimen may be required situations with increased risk of resistance: recent antibiotic therapy (months), inflammatory bowel disease with recent antibiotic exposure, international travel, or prolonged hospitalization. In these cases, the addition of an aminoglycoside should be considered.

For patients who have a history of an allergic reaction to antibiotics, it is important to obtain a detailed allergy history as outlined in the Cefazolin Safety Checklist (or flowsheet). Severe anaphylactic type 1 reactions are not common in patients receiving antibiotics: 0.01-0.05% in patients receiving penicillin and 0.0001-0.1% for cephalosporins so it is safe to prescribe cephalosporins in most patients who are said to have a drug allergy¹⁰. A significant allergy is defined as a prior allergic reaction (or positive skin testing) with resultant hospitalization or anaphylaxis (hypotension, laryngeal edema, wheezing, angioedema, urticaria). Such patients should not receive the same drug or other penicillins if anaphylactic to penicillin. The rate of cross-reactivity between penicillin and cephalosporins depends on the similarity of side chains but is uniformly much less than the commonly cited 10% and is exceedingly unlikely for cefazolin¹⁰. If a patient has a history of severe non-IgE mediated reaction (e.g. serum sickness), an alternative antibiotic

should be prescribed. For patients with a severe β -lactam allergy, vancomycin should be used instead of a cephalosporin. Non-severe reactions/side effects such as mild maculopapular rash and gastrointestinal upset are NOT reasons for prescribing clindamycin or vancomycin.

To reduce surgical site infections, antibiotic prophylaxis must attain adequate tissue concentration at the time of incision and be maintained during the procedure. To achieve this objective, antibiotics directed against the most common contaminating bacteria must be administered within 60 minutes before incision at the correct dose. Vancomycin and fluoroquinolones require a longer infusion time and should be initiated to ensure completion within 60 minutes of incision. In Caesarean section, prophylaxis should be given prior to incision rather than after cord clamping to reduce maternal infections¹¹.

Additionally, re-dosing of antibiotics for prolonged procedures is necessary to maintain adequate tissue concentration. Thus, additional intraoperative doses are recommended at intervals approximating two times the half-life of the antibiotic or if there is significant blood loss (>1.5L) for all antibiotics except vancomycin¹². The re-dosing interval should be measured from the time of antibiotic administration, not the incision time. Re-dosing may not be required in patients with renal insufficiency.

Regarding dosages, these guidelines have included a dose for cefazolin of 3g for patients weighing more than 120kg. This recommendation is based on expert opinion and the safety profile of cefazolin. The bariatric and obstetrical surgery literature suggests, although not consistently, that there are suboptimal tissue concentrations with 2g of cefazolin in patients weighing more than 120kg. However, there is no strong evidence of decreased SSIs with higher dosing. Vancomycin should be given as 15 mg/kg rounded to the nearest 250mg (max 2g/dose) using total body weight. Aminoglycoside dosing should be based on a dosing weight calculation if the patient's actual body weight is > 20% above the ideal body weight and rounded to the nearest 20mg (Table 1). An increase in routine aminoglycoside prophylaxis dosing to 5mg/kg is not recommended. Other guidelines recommend this higher dose for all patients based on results from a single center study¹³ In procedures lasting more than 3.5 hours, there were fewer SSIs with high dose gentamicin (4.5mg/kg compared to 1.5mg/kg). However patients with kidney injury were excluded and gentamicin was not re-dosed in the 1.5mg/kg group. Therefore, we have recommended intraoperative re-dosing in those with normal kidney function instead of using the higher dosing.

Postoperative prophylaxis is not recommended. This is in keeping with the systematic review performed by the WHO Global Guidelines (2016) which included 44 RCTs comparing the same antibiotic given as a single preoperative dose with prolonged postoperative continuation of prophylaxis. When the results of forty of these trials were combined, there was no significant difference in the SSI rates when antibiotics were continued post-operatively (OR 0.89, 95% CI: 0.77–1.03).¹

When stratified by procedure, postoperative prophylaxis may decrease SSIs in cardiac, vascular, and orthognathic surgeries. In cardiac surgery, there is low quality evidence to support giving 24 hours of postoperative antibiotics. Tamayo et al (2008) compared a single dose to 24 hours of prophylaxis and found a significant difference in SSIs (8.3% and 3.6% respectively $P=0.004$),¹⁴ but no difference in organ-space infections, duration of hospitalization, or mortality. There is no evidence to support the continuation of antibiotics after 24 hours for cardiac surgery (OR: 0.74; 95% CI:0.32–1.73). In the trial by Nooyen et al, a single dose of cefuroxime was compared to a three-day course postoperatively and no difference in sternal infection was found (14% and 13% respectively). However, patients were only followed for 7 days¹⁵. In vascular surgery, there is a single RCT comparing a single dose of prophylaxis with a multiple dose regimen until the lines/drains were removed up to a maximum of 5 days).¹⁶ While there was a decrease in wound infection from 18% to 10% ($p=0.041$; RR = 2.00, 95% CI: -1.02 to 3.92), no difference in graft infection was found at 42 days follow-up.

Given the low quality of evidence, risk of antimicrobial resistance, and *Clostridium difficile* we do not recommend postoperative prophylaxis in any patient population. This recommendation also applies to pediatrics although there are no studies including this population.

Similarly, antibiotic prophylaxis should not be continued post-operatively if drains, catheters, or lines are left in place. In the WHO Global Guidelines, a systemic analysis of seven RCTs comparing single dose

prophylaxis with postoperative continuation did not find any reduction in SSIs with prolonged antibiotics for such devices (OR: 0.79; 95% CI: 0.53–1.20).¹

MRSA colonized patients should receive vancomycin as part of the prophylactic regimen. Unlike cefazolin, vancomycin has no activity against Gram-negative organisms. When Gram-positive microorganisms are the only concern for infection, adding cefazolin to vancomycin is usually unnecessary. However, most guidelines recommend using cefazolin in addition to vancomycin for MRSA colonized patients to decrease SSIs in cardiac, vascular, and orthopedic/spinal surgeries. It is suspected that vancomycin is less effective for MSSA than β -lactams¹⁷⁻²⁴. However, data to support this recommendation are inconsistent and largely observational. Furthermore, there is an increased likelihood of transient renal injury with dual agent prophylaxis²⁵.

2. Perioperative normothermia

2.1 Active measures should be taken to ensure that the patient's body temperature is greater than 36°C perioperatively

2.1.1 If the patient is at high risk of hypothermia or if his/her temperature is less than 36°C preoperatively, forced-air warmers should be started prior to induction to ensure a body temperature greater than 36°C prior to surgery

2.2 The use of forced-air warming systems and warmed IV and irrigation fluids should be used intraoperatively to maintain body temperature greater than 36°C for patients during the surgical procedure

2.2.1 Warming systems should not be used in patients undergoing surgery where intraoperative hypothermia is intended (i.e. off-pump surgery)

General and neuraxial anesthesia impairs thermoregulatory control. As a result, nearly all unwarmed surgical patients become hypothermic if active measures are not taken to maintain normothermia. Heat loss occurs from rapid core-to-peripheral redistribution of body heat and is followed by a reduction in core temperature that results from heat loss exceeding heat production. The typical rate of heat loss leads to a drop in body temperature of 1 to 1.5° C during the first hour of general anesthesia.

Hypothermia increases the risk of surgical site infections through one of two mechanisms. First, thermoregulatory vasoconstriction reduces subcutaneous oxygen tension, and tissue oxygen tension correlates highly with infection risk. Mild core hypothermia also impairs immune function through impairment of including T-cell-mediated antibody production and neutrophil oxidative killing. Typically, patients undergoing major surgery without directed attention to the maintenance of normothermia will have core temperatures near 34.5°C at the completion of operation. This degree of hypothermia is associated with a threefold incidence of surgical site infections after colon resection.²⁶ Mild perioperative hypothermia has also been causally linked to numerous complications including increased blood loss, adverse cardiac events, prolonged post-anaesthetic recovery and hospitalization. In the review by the WHO guidelines, pre- and intraoperative body warming significantly reduced SSIs compared to no warming (OR: 0.33; 95% CI: 0.14-0.62).¹

Normal core temperature can be maintained during surgery through use of active measures including warmed intravenous fluids and inspired gases as well as forced air warming. The latter involves an air blanket placed over the patient that circulates air warmed to 40° C. Water blankets may also be used, but are not as effective in maintaining body temperature. Patient temperature can be monitored using conventional thermometer probes, with active measures adjusted to maintain core temperature near 36.5° C. Any method or combination of methods that maintains the target core temperature appears to have the same effect.²⁷

Resources including warming blankets, head covers, warmed IV fluids and reliable thermometers must be readily accessible. Any irrigation fluids used in a surgical procedure should be at or slightly above body temperature before use. The OR should be kept in the range of 20° C, a compromise between what is

acceptable for the patient and tolerable for the surgical team. Forbes et al. (2009) developed a guideline on the prevention of perioperative normothermia²⁸. The authors conducted a systematic review of the literature from 1950-2008 with one of the aims being to determine whether warming devices help to maintain core body temperature. Overall, eight RCTs of good or fair quality were included. The authors found that there was fair, level I evidence to recommend the use of IV fluid warmers for abdominal procedures > 1 hour as well as fair, level I evidence to recommend the use of warmed forced air preoperatively as well as intraoperatively when procedures are expected to last > 30 minutes. These recommendations are mirrored in the National Institute for Health and Care Excellence (NICE) guidelines that were published in 2008. NICE recommends that if the patient's temperature is below 36°C prior to the operation, forced air warming should be started preoperatively and maintained throughout surgery. They recommend that the patient's temperature should be 36°C or above before the induction of anesthesia. Intraoperatively, it is recommended that the operating room should be kept at 21°C while the patient is exposed and until the forced air warming is established. Additionally, the patient should be covered throughout the procedure and exposed only during surgical preparation. IV fluids and blood products should be warmed to 37°C using a fluid warming device. Irrigation fluids should be warmed to 38-40°C. NICE recommends that all patients, including high risk patients, should be warmed intraoperatively from induction of anesthesia using a forced air warming device, regardless of the length of surgery. Lastly, it is recommended that patients should not be transferred to the ward unless the patient's temperature is 36°C or above. If the patient's temperature is below 36°C postoperatively, he/she should be warmed using forced air warming.²⁷

Since the publication of these guidelines, several meta-analyses have been conducted to determine the optimal warming system. A Cochrane Review was conducted by Madrid et al in 2016 to compare warming systems aimed at maintaining normothermia through skin contact.²⁹ The authors included 67 RCTs with a total of 5,438 participants. The review included all elective surgeries except where hypothermia was needed. Three trials which included 589 participants showed a significant benefit of forced-air warming over control in decreasing the rate of SSI and wound complications (wound healing and dehiscence) (RR 0.36, 95%CI 0.20 to 0.66, p=0.0008). One trial (n=59) assessed forced air compared to electric heating and found no significant difference (RR 1.03, 95%CI 0.07-15.77, p=0.98). Three trials (208 participants) compared forced-air vs. warm-water circulation system and found no statistically significant difference (RR 3.00, 95%CI 0.62 to 14.53, p=0.17). Overall, the Cochrane review found that forced-air warmers reduced the rate of SSIs as compared to other warming systems. In addition, there is a risk of skin burns with conductive warming mattresses.

Another meta-analysis was conducted in 2016 by Nieh et al assessing the effectiveness of forced-air warming for prevention of perioperative hypothermia in surgical patients.³⁰ The authors included 36 trials. Five trials assessed forced-air warmer vs passive insulation. These trials had high heterogeneity. Using a fixed effects model, the forest plot showed an overall standardized mean difference (SMD) of 0.461°C (95%CI 0.244 to 0.678, p<0.001) indicating that forced air warmers were superior. Five trials with high heterogeneity compared forced-air warmers vs. resistive heating blankets and using a random-effects model, the forest plot showed an overall SMD of -.144°C (95%CI -0.677 to 0.390, p=0.598) indicating no difference. Five trials with high heterogeneity looked at forced-air compared to radiant warming systems and under a random-effects models, the forest plot showed an overall SMD of -0.253°C (95%CI -1.054 to 0.547; p=0.535) indicating no difference in the effectiveness. Three trials compared forced-air to circulating-water mattresses. The trials were again highly heterogeneous and using a fixed-effects model, the forest plot showed an overall SMD of 0.966°C (95%CI 0.531 to 1.400; p<0.001) indicating that forced air was more effective than circulating water mattresses. Three trials with high heterogeneity compared forced air and circulating water garments and under a random-effects model, the forest plot showed an

overall SMD of -1.186°C (95%CI -3.774 to 1.402 , $p=0.369$) indicating similar effects. Overall, these authors also found support for the use of forced-air compared to other warming systems.

With respect to warming of IV and irrigation fluids, Campbell et al conducted a Cochrane review in 2015, including RCTs or quasi-RCTs evaluating the effectiveness of pre- and/or intra-operative warming of IV and irrigation fluids in preventing perioperative hypothermia and its complications during surgery. Twenty-four studies including 1250 patients provided moderate quality evidence. Overall, the authors found that warmed IV fluids kept the core temperature of participants approximately 0.5 degree warmer than patients with room temperature fluid infusion. There was no statistically significant difference in core body temperature or shivering between warmed and room temperature irrigation fluids.³¹

While the above literature was conducted in adult patients, the WHO guidelines also consider these recommendations applicable to pediatric surgical patients.

3. Preoperative skin preparation

3.1 Patients should be prepped with alcohol-based chlorhexidine gluconate (2% chlorhexidine gluconate and 70% isopropyl alcohol) with the following exceptions:

3.1.1 Povidone iodine should continue to be used for ophthalmic procedures and those involving the inner ear or mucous membranes

3.1.2 Procedures where there is no time for alcohol solutions to dry (eg: in trauma), an aqueous-based antiseptic solution should be used and allowed to dry

3.1.3 Infants less than 2 months old

3.2 Alcohol-based antiseptics are flammable in operative procedures involving electrosurgery (i.e. electrocautery) so pooling on drapes and the patient should be avoided. The antiseptic solution should also be allowed time to dry completely (~ 3 minutes, longer in areas with excess hair) to limit fire hazard

3.3 Patients should bathe or shower the entire body and head prior to surgery using plain or antimicrobial soap

The recommendation for the use of chlorhexidine gluconate is based on a 2010 meta-analysis of 6 studies containing 5,031 patients undergoing clean-contaminated general or gynaecological surgery to determine whether chlorhexidine alcohol was more effective than povidone-iodine in reducing the risk of SSIs. Chlorhexidine alcohol was superior compared with povidone-iodine (pooled odds ratio 0.68, 95% CI 0.50-0.94, $p=0.019$). The authors concluded that chlorhexidine should be used preferentially over povidone-iodine³².

In addition, a recent large, multi-centre trial which included 849 patients who underwent clean-contaminated surgery (colorectal, small intestinal, gastroesophageal, biliary, thoracic, gynaecologic, urologic) were randomized to have their skin scrubbed with 2% chlorhexidine gluconate and 70% isopropyl alcohol ($n=391$) or scrubbed and painted with 10% povidone-iodine ($n=422$). The overall rate of SSIs was significantly lower in the chlorhexidine alcohol group (9.5% vs 16.1%, $p=0.004$; relative risk, 0.59; 95% CI, 0.41-0.85). As well, chlorhexidine/70% alcohol performed better in preventing superficial incisional infections (4.2% vs 8.6%, $p=0.008$) and deep incisional infections (1% vs 3%, $p=0.05$). There was no difference in organ-space infections (4.4% vs. 4.5%). The authors concluded that chlorhexidine/70% alcohol is far superior to povidone-iodine for use in clean-contaminated surgery³³.

Although these recent studies have demonstrated decreased risk of SSIs with the use of chlorhexidine/70% alcohol, many are still concerned about the safety of 70% alcohol due to a risk of fire in the operating room. Although one study commented that the use of alcohol-based products does pose a small risk of risk of fire³³, this risk is due to using large 26ml applications which therefore takes longer to dry, increases the risk of pooling in drapes and soaking in hair. A small amount of chlorhexidine/70% alcohol is safe if it is used appropriately (adequate drying time, avoidance of pooling and soaking of hair)³⁴. It is recommended

that an educational program be implemented to ensure safe application of chlorhexidine/70% alcohol before its implementation. Chlorhexidine use should follow manufacturer's instructions including avoidance of contact with eyes, middle ear, mucous membranes, and meninges (including lumbar puncture). In addition, should avoid for infants less than 2 months old. Alcohol containing products should not be used on mucous membranes or eyes.

A Health Canada review found topical, non-prescription chlorhexidine products may cause serious allergic reactions. There may be increased risk of anaphylaxis when using chlorhexidine in the mouth, on open wounds, or immediately before or during surgery.³⁵

This evidence is for adult patients and no studies were available for the pediatric population to make a recommendation.

Bathing or showering prior to surgery to clean the skin is considered good clinical practice. There is no definitive evidence to support the use of antimicrobial soap (chlorhexidine) compared to plain soap to reduce SSIs. Webster and Osborne conducted a Cochrane review in 2015 comparing preoperative bathing or showering using any antiseptic preparation with non-antiseptic preparations.³⁶ Seven RCTs were included with 10,157 patients. Overall, there was no reduction in SSI rates associated with preoperative washing with chlorhexidine compared to other wash products. Three trials (7791 participants) compared chlorhexidine 4% with placebo and found no statistically significant difference in SSIs (chlorhexidine 9.1% vs placebo 10.0%; RR 0.91, 95%CI 0.80-1.04). Three trials totalling 1443 patients compared chlorhexidine to bar soap and found no significant difference (RR 1.02, 95%CI 0.57-1.84). An independent systemic review by the WHO Global Guidelines confirmed these results.¹

While there are no studies in pediatric patients, the above recommendation for bathing applies to this population as well. However, manufacturer's instructions should be followed if antimicrobial soap is used.

4. Preoperative hair removal

4.1 Hair removal should not be performed for the purposes of SSI prevention. If hair removal is necessary, clippers should be used

Preoperative preparation for surgery has traditionally included the removal of body hair from the intended surgical site. This practice developed for two purposes: 1) to reduce the inconvenience of hair in the surgical field; and 2) to reduce the risk of SSI. However, several lines of evidence have challenged this practice and current data suggest that hair removal might increase SSI rates³⁷⁻³⁹. If hair removal is required for technical reasons, there is evidence to suggest that the timing and manner of hair removal might significantly affect the rates of SSI. When hair removal is required, it should be performed with a clipper rather than a razor just prior to application of the skin prep. The increased SSI risk associated with shaving has been attributed to microscopic cuts in the skin that later serve as foci for bacterial multiplication.

A Cochrane review was conducted by Tanner et al in 2011 to determine if routine pre-operative hair removal and the timing or method of hair removal influenced the rate of SSIs. Fourteen trials were included in the review. Six trials totalling 972 participants compared hair removal (shaving, clipping, or depilatory cream) with no hair removal and found no statistically significant difference in SSI rates. Three trials with 1343 participants compared clipping to shaving and showed significantly more SSIs associated with shaving (RR 2.09, 95% CI 1.15 to 3.80). Seven trials (1213 participants) found no significant difference in SSI rates when hair removal by shaving was compared with depilatory cream (RR 1.53, 95% CI 0.73 to 3.21). Lastly, one trial compared two groups that shaved or clipped hair on the day of surgery compared with the day before surgery and showed no statistically significant difference in the rate of SSIs between groups. Thus, the authors concluded that when it is necessary to remove hair, clippers are associated with fewer SSIs than razors.⁴⁰

The evidence for neurosurgical procedures and hair removal is slightly different as many patients dread having their hair removed. However, some surgeons believe that hair removal is necessary to facilitate

accurate planning of the incision, attachment and/or removal of the drapes as well as for closing the wound. Thus, Broekman et al conducted a systematic review of the literature to assess the evidence for preoperative shaving for adults and children including craniotomies, burr hole procedures, spine surgery or implantation surgery⁴¹. The authors found 21 studies that met their inclusion criteria which involved 11,071 patients. Only two of the studies were RCTs and the quality of included studies was low. Due to the nature of the studies, a meta-analysis was not feasible. Overall, the authors found no evidence to support pre-operative shaving. Additionally, some studies suggested that preoperative shaving may increase the chance of SSIs. However, due to the low quality of evidence, this recommendation is weak at best.

There has been no evaluation of differing strategies to change practice. It is generally believed that education and institutional policy development in concert with a) assuring the ready availability of clippers and b) removal of razors from the operating room environment might be effective. Patients should either be explicitly asked not to shave or be requested to ask their physicians before any hair removal is considered given the belief among many patients that shaving preoperatively is necessary.

While there are no studies in pediatric patients, the above recommendations apply to this population as well.

5. *Staphylococcus aureus* decolonization

5.1 In cardiac surgery and orthopedic/spinal surgery with hardware insertion, *Staphylococcus aureus* screening with nasal swab and decolonization of carriers with intranasal mupirocin 2% ointment BID and chlorhexidine-gluconate body wash for 5 days before surgery should be considered

5.2 For MRSA carriers, decolonization in conjunction with hospital infection control practitioners or infectious disease consultants should be considered

S. aureus is the most common cause of SSIs and patient colonization is a risk factor for infection. Screening for carriers of methicillin-resistant *S. aureus* (MRSA) or methicillin-susceptible *S. aureus* (MSSA), and subsequent decolonization with mupirocin and chlorhexidine can decrease SSIs for cardiac, spine, and orthopedic procedures.⁴² Currently, there is less evidence available for other surgical procedures. As outlined below, studies have shown a decrease in *S. aureus* infections among patients with low mupirocin resistance. However, there is concern of increasing resistance with more mupirocin use so sensitivities should be monitored. Decolonization of patients without *S. aureus* screening is not recommended because of decreased efficacy and increased resistance.

This recommendation is not applicable to pediatric patients as studies were only conducted in adults.

There was some benefit in a randomized, double-blind, placebo-controlled trial using intranasal 2% mupirocin ointment for up to 5 days before general surgery, neurosurgery, and cardiothoracic surgery procedures⁴³. Overall, 2.3% of mupirocin recipients and 2.4% of placebo recipients developed *S. aureus* SSI. Among patients with nasal carriage of *S. aureus*, mupirocin decreased *S. aureus* nosocomial infections from 7.7% to 4.0% (OR 0.49; 95% confidence interval, 0.25-0.92; P=0.02). However, there was no significant difference in *S. aureus* SSIs specifically (3.7% for mupirocin; 5.9% for placebo). The rates of mupirocin resistance and MRSA were low (<1%) in the study population.

In another randomized double-blind, placebo-controlled trial, *S. aureus* nasal carriers were decolonized with 2% mupirocin nasal ointment and chlorhexidine soap for 5 days⁴⁴. Deep surgical site infections were significantly reduced (0.9% decolonization; 4.4% placebo; RR 0.21; 95% CI, 0.07-0.62). All the *S. aureus* strains isolated in this study were susceptible to methicillin and mupirocin. The trial included patients having cardiothoracic surgery (n=391), orthopaedic (n=172), vascular surgery (n=95), general surgery (n=107), and gastrointestinal surgery (n=43).

In a time-series analysis of patients undergoing cardiac surgery or hip/knee arthroplasties, rates of *S. aureus* SSIs were compared before and after implementation of a bundle in which *S. aureus* carriers were decolonized with mupirocin and chlorhexidine-gluconate for up to 5 days before surgery and predefined perioperative prophylaxis (MRSA carriers received vancomycin and cefazolin or cefuroxime; all others received cefazolin or cefuroxime)⁴⁵. Implementation of the bundle was associated with a significant reduction in complex *S. aureus* SSIs (OR= 0.60; 95% CI, 0.37-0.98). There was minimal resistance to mupirocin and MRSA colonization was approximately 3.5-4.3%.

In patients undergoing elective joint arthroplasty, decolonization of patients with positive MRSA or MSSA nasal swabs (3% and 25% respectively) was associated with a significant reduction in SSIs from 1.11% before screening to 0.34% after implementation⁴⁶.

The WHO Global Guidelines performed a systematic review of 6 RCTs including 2385 *S. aureus* colonized patients that compared mupirocin (with or without chlorhexidine body wash) to placebo/no treatment. There was a significant reduction in SSIs caused by *S. aureus* (OR 0.46; 95% CI: 0.31-0.69). Most studies included cardiothoracic and orthopedic surgery. However, there may also be benefit in other types of surgery based on regression analysis.

Cost-benefit analysis suggests screening and decolonization of *S. aureus* carriers undergoing cardiothoracic and orthopaedic surgery lowers hospital costs⁴⁷.

6. Special considerations

6.1 Antimicrobial-coated sutures may be used to reduce SSIs

There is low to moderate evidence showing antimicrobial sutures reduce SSIs. The WHO reviewed 18 studies (13 RCTs, 5 cohort studies) comparing antimicrobial- with non-coated sutures. There was moderate quality for RCT trials (OR: 0.72, 95% CI: 0.59-0.88) and low quality for observational studies (OR: 0.58, 95% CI 0.40-0.83) in reducing SSIs. Most studies included triclosan-coated sutures. Further studies are required to evaluate the effect on wound healing, antimicrobial resistance, and risk of contact allergy.¹

Most studies included adults but this recommendation may be applied to pediatrics if there is no contraindication in the manufacturer's instructions.

6.2 Local application of vancomycin powder in spine surgery is controversial and no strong recommendation can be made with the current evidence

The use of intraoperative local vancomycin powder, in addition to preoperative systemic antibiotics, for spinal surgery is controversial. Only one RCT has been performed showing no difference in SSI rates (vancomycin powder: 1.61%; no powder: 1.68%)⁴⁸. This study included 907 patients, 594 with instrumented surgery, but no sample size calculation was performed. In addition, risk factors like BMI and smoking were not analyzed.

A systemic review and meta-analysis of principally retrospective studies did show a reduction in superficial or deep infections with intrawound vancomycin (OR 0.43; 95% CI 0.22-0.82; p=0.01)⁴⁹. However, this analysis did not evaluate the risk of bias for each study. In addition, there was heterogeneity among the included trials that was not explored with subgroup analyses⁵⁰. Two other reviews found vancomycin reduces SSI (OR 0.16; 95% CI 0.09–0.30)⁵¹ (OR 0.34 95% CI 0.17–0.66)⁵². As outlined in other reviews, this evidence is low quality because of the limitations in sample size, population, study designs and outcome measures^{53,54}.

Additional retrospective studies since these reviews support vancomycin powder use in instrumented procedures^{55,56} and high-risk patients such as diabetics or revisions⁵⁷. Therefore, specific high-risk populations may benefit from vancomycin powder.

While most studies did not find complications from vancomycin powder, there are concerns of allergic reaction, antimicrobial resistance, suprathreshold exposure with systemic effects, seromas, and impaired bone healing and union.

Large prospective RCTs are required before a recommendation can be made for vancomycin powder use. There are no guidelines for its use at this time.

6.3 Antibiotic impregnated shunts may be beneficial in reducing central nervous system shunt infections but no strong recommendation can be made with the current evidence

A multicenter, prospective RCT found positive CSF cultures were less frequent in adult patients with external ventricular drains (EVD) containing minocycline and rifampin compared to standard catheters (1.3% compared with 9.4%, respectively, $p = 0.002$)⁵⁸. In a prospective RCT fewer shunt infections were found in ventriculoperitoneal shunts impregnated with clindamycin and rifampin than standard shunts for hydrocephalus (6% vs 16.7% respectively)⁵⁹.

A Cochrane analyses of these 2 RCTs found an OR of 0.21 (95% CI 0.08 to 0.55) but conclude this evidence is limited by the low number of studies and participants⁶⁰.

Reviews of primarily retrospective studies have found low to moderate quality of evidence for antibiotic impregnated shunts in reducing shunt infections for studies including both adult and pediatrics (RR 0.46%, 95% CI 0.33-0.63)⁶¹ and pediatrics alone (RR 0.51 (95% CI 0.29–0.89)⁶².

A meta-analysis of 4 RCTs and 4 nonrandomized prospective studies found lower rates of CSF infection (OR 0.25, 95% CI 0.12 to 0.52, $P < 0.05$) in antimicrobial impregnated EVDs compared to standard catheters⁶³.

The ASHP guidelines do not recommend routine use of antibiotic impregnated devices until more well-designed studies are performed.

6.4 Endocarditis prophylaxis is only required in patients with a few predisposing cardiac conditions prior to specific dental procedures and manipulation of the respiratory mucosa.

A full review of the evidence for infective endocarditis (IE) prophylaxis is beyond the scope of this document and has been reviewed elsewhere⁶⁴. In summary, only a few predisposing cardiac conditions may require prophylaxis: prosthetic cardiac valve or prosthetic material used for cardiac valve repair, previous IE, cardiac transplantation recipients who develop cardiac valvulopathy, and congenital heart disease (unrepaired cyanotic congenital heart disease, including palliative shunts and conduits; or completely repaired congenital heart defect with prosthetic material or device, whether placed by surgery or by catheter intervention, during the first 6 months after the procedure; or repaired congenital heart disease with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device).

In patients with these conditions, prophylaxis is recommended prior to dental procedures involving manipulation of gingival tissue, dental periapical regions, or perforating the oral mucosa. Prophylaxis may be considered for invasive procedures of the respiratory tract that involves incision or biopsy of the respiratory mucosa, such as tonsillectomy and adenoidectomy. Prophylaxis is not required in gastrointestinal or genitourinary procedures to prevent IE.

Despite these recommendations, most bacteremias result from routine daily activities (i.e. chewing food, tooth brushing). Consequently, there should be greater focus on dental care and oral health.

Table 1. Procedure specific recommended agents and duration

Division	Recommended Agents	B-lactam allergy Recommended agents
Cardiac		
Coronary artery bypass (CABG), valve replacement (+/- CABG), other cardiac procedures	cefazolin	vancomycin
Ventricular assist devices, Device insertion (e.g. pacemaker)	cefazolin	vancomycin
Cardiac catheterization, Transesophageal echocardiogram	None	None
General		
Gastroduodenal/esophageal/ distal pancreatic resection	cefazolin	vancomycin + aminoglycoside
Percutaneous endoscopic gastrostomy (PEG)	cefazolin	vancomycin + aminoglycoside
Biliary tract- laparoscopic procedure- Elective low risk	None	None
Biliary tract- laparoscopic procedure – High risk emergency, inserting prosthetic device, diabetes, risk of intraoperative gallbladder rupture/conversion to open, age >70 years, ASA ≥3, reintervention within 1 month, acute cholecystitis, obstructive jaundice, CBD stones, nonfunctional GB, pregnancy, immunosuppression	cefazolin	vancomycin + aminoglycoside
Biliary tract- open procedure		
Liver resection		
Colorectal, small bowel, appendectomy Pancreaticoduodenectomy ^{b,c}	cefazolin + metronidazole If risk of Gram-negative resistance: add aminoglycoside	Vancomycin ^a + aminoglycoside + metronidazole
Hernia repair- Hernioplasty, herniorrhaphy	cefazolin	vancomycin
Low risk anorectal procedures: hemorrhoidectomy, fistulotomy, sphincterotomy	None	None
Thoracic		
Non-cardiac procedures (e.g. lobectomy, pneumonectomy, lung resection, and thoracotomy) Video-assisted thorascopic surgery	cefazolin	vancomycin
Thoracentesis or chest tube insertion for non-traumatic indications (e.g. spontaneous pneumothorax) Mediastinoscopy	None	None
Head and neck		

Division	Recommended Agents	B-lactam allergy Recommended agents
Clean: no incision through oral/nasal/pharyngeal mucosa (e.g. parotidectomy, thyroidectomy, and submandibular gland excision)	None	None
Clean with placement of prosthetic material (excludes tympanostomy tubes)	cefazolin	vancomycin + metronidazole ^d
Clean-contaminated (incision through oral/pharyngeal mucosa): cancer surgery and other clean-contaminated procedures with the exception of tonsillectomy and functional endoscopic sinus procedures	cefazolin + metronidazole	vancomycin + aminoglycoside + metronidazole ^e
Neurosurgery		
Elective craniotomy, stereotactic brain biopsy, cerebrospinal fluid-shunting procedures, ICP monitor, external ventricular drain, and implantation of intrathecal pumps	cefazolin	vancomycin
Endoscopic transsphenoidal neurosurgery	Cefazolin	Vancomycin + aminoglycoside (There is a minimal data for the best regimen in such patients)
Orthopedic		
Arthroscopy without graft implantation	None	None
Spinal procedures with and without instrumentation, hip fracture repair, Implantation of internal fixation devices (e.g., nails, screws, plates, wires) and total joint replacement	cefazolin	Vancomycin If emergent surgery precludes the infusion time for vancomycin, clindamycin may be used instead
Urologic		
Prior to stone removal or invasive procedures involving mucosal bleeding/trauma, obtain urine sample and treat based on culture and sensitivity result		
Cystoscopy/Shock wave lithotripsy <ul style="list-style-type: none"> no risk factors 	None	
Cystoscopy/Shock wave lithotripsy: <ul style="list-style-type: none"> Risk factors: advanced age, immunocompromised, large stone burden, history of pyelonephritis/infected stone, prolonged catheterization, nephrostomy tubes 	If no hospitalization in last year, recent antibiotic use from the class, or other risks for resistance: ciprofloxacin 500mg PO or cefazolin (if no beta-lactam allergy)	

Division	Recommended Agents	B-lactam allergy Recommended agents
<ul style="list-style-type: none"> Manipulation: Prostatectomy, biopsy, foreign body removal, urethral dilation, stent placement/removal Ureteroscopy Percutaneous nephrolithotomy Transrectal prostate biopsy ^f	If risk of Gram-negative resistance: aminoglycoside or ceftriaxone 1g (if no beta-lactam allergy)	
Percutaneous renal surgery	cefazolin	vancomycin
Open or Laparoscopic: without entry into bowel/vagina	cefazolin	vancomycin + aminoglycoside ^g
involving manipulation of bowel/vagina	cefazolin + metronidazole	vancomycin + aminoglycoside + metronidazole ^a
Vascular		
Brachiocephalic procedures and carotid endarterectomy without prosthetic material Angiography, angioplasty, thrombolysis, vascular stenting	None	None
Arterial surgery Graft placement or repair	cefazolin	vancomycin
Plastics		
Clean without risk factors (not breast surgery)	None	None
Clean - high risk <ul style="list-style-type: none"> prosthetic material, skin irradiation, traumatic/crush hand injuries, flap reconstruction, panniculectomy, injuries requiring amputation/reconstructive limb surgery, injuries involving bone, joint, tendon (except open flexor tendon injuries) or nerve Clean-contaminated	cefazolin	vancomycin
Breast surgery	cefazolin	vancomycin
Ophthalmic		
	<u>1 drop every 5-15 min for 5 doses:</u> Topical neomycin-polymyxin B-gramicidin or gatifloxacin or moxifloxacin Optional to add at the end of the procedure: subconjunctival injection cefazolin 100mg or intracameral cefazolin 1-2.5mg or cefuroxime 1 mg	
Obstetrical/Gynecological		
Caesarean section ^h	cefazolin	aminoglycoside + Vancomycin

Division	Recommended Agents	B-lactam allergy Recommended agents
Hysterectomy	cefazolin	vancomycin + aminoglycoside ⁱ
Therapeutic termination of pregnancy	Doxycycline 100 mg PO 1 hour before procedure, then 200 mg PO post-procedure	

^a ASHP recommends numerous regimens in Beta-lactam allergic patients. We have avoided using clindamycin and added vancomycin to the recommended aminoglycoside and metronidazole regimen because Gram-positive organisms including *S. aureus* are common causes of SSIs (Blumetti Surgery 2007 142:704–711; Hidron Infection Control and Hospital Epidemiology, Vol. 29, No. 11 (November 2008), pp.996-1011)

^b The addition of metronidazole for pancreaticoduodenectomy is controversial and not in the ASHP guidelines. However, these surgeries are high risk for infection, involve bowel manipulation, anaerobic coverage is used in other centers (Fong JAMA Surg. 2016;151(5):432-439), and *Bacteroides* spp. are isolated in SSIs (Sugiura World J Surg (2012) 36:2888–2894; Sudo World J Surg (2014) 38:2952–2959).

^c There is a strong association of preoperative biliary stenting with bacteriobilia (OR 725.3 [95% CI 155.6-3380.5]; $P < .001$), which in turn is strongly associated with postoperative wound infection (OR 2.5 [95% CI 0.583-11.05]; $P = .05$) (Fong JAMA Surg. 2016;151(5):432-439).

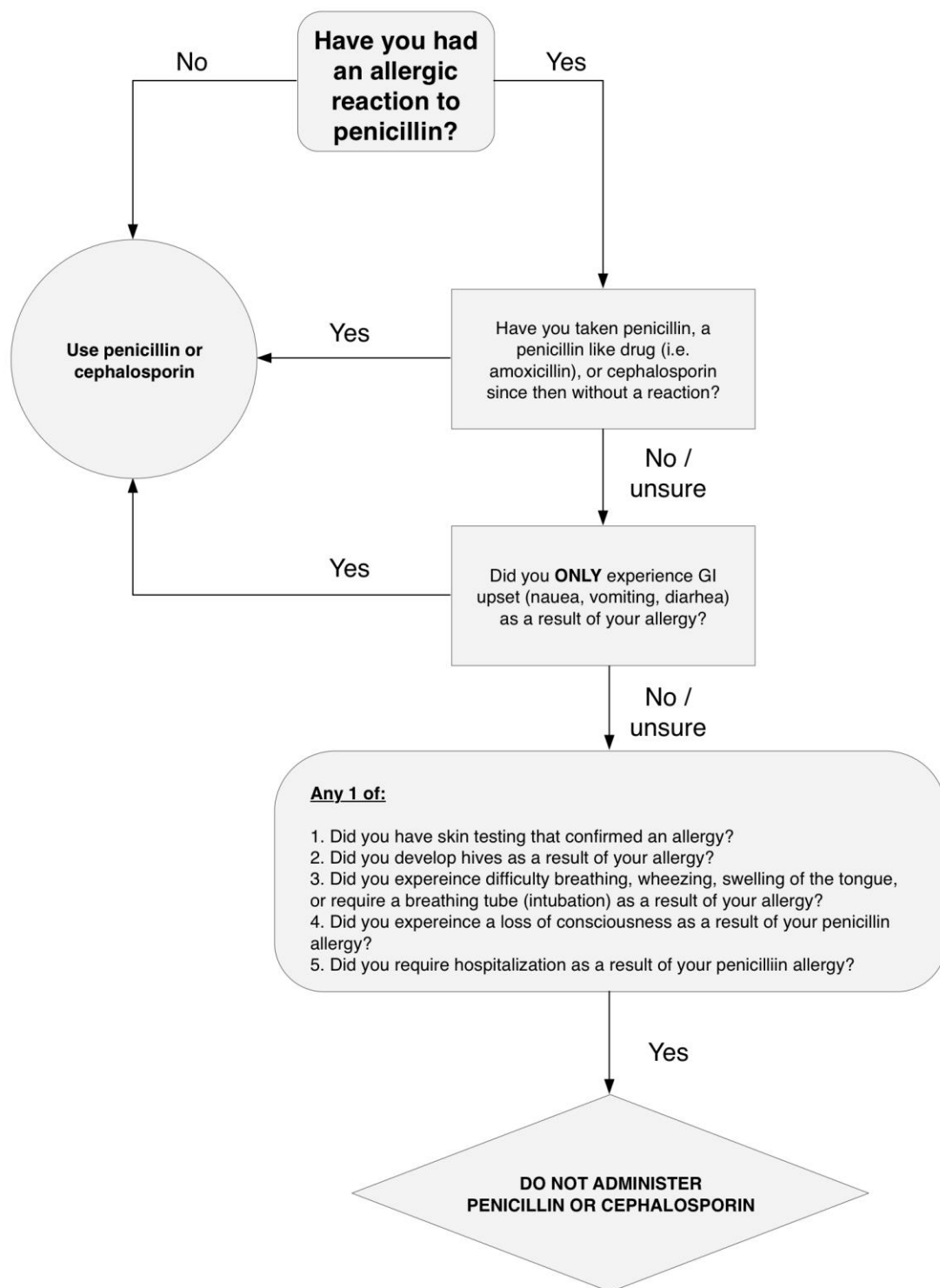
^{d,e} The ASHP guidelines recommend clindamycin for Beta-lactam allergic patients in head and neck surgery. Clindamycin prophylaxis is associated with higher SSIs in head and neck free flap surgeries (Durand Laryngoscope, 125:1084–1089, 2015, Mitchell JAMA Otolaryngol Head Neck Surg. 2015;141(12):1096-1103), major ablative head and neck resection with free tissue transfer (Pool et al Otolaryngology–Head and Neck Surgery 2016, Vol. 154(2) 272–278), laryngectomy for larynx cancer (Langerman Otolaryngology–Head and Neck Surgery 2015, Vol. 153(1) 60–68), and other head and neck oncologic surgery (Weber Arch Otolaryngol Head Neck Surg. 1992;118:1159-1163; Langerman Otolaryngology–Head and Neck Surgery 2016, Vol. 154(6) 1054–1063). There is also a higher risk for *C. difficile* infections with clindamycin (Langerman Otolaryngology–Head and Neck Surgery 2015, Vol. 153(1) 60–68).

^f The risk of infection after transrectal prostate biopsy is high because of the nature of the procedure and increasing resistance patterns of *E. coli*, particularly for fluoroquinolones and 1st generation cephalosporins. Patients with increased risk of harboring resistant organisms (recent antimicrobials, infections, travel), should have perirectal culture swab performed prior to biopsy according to the Canadian Urological Association to guide prophylaxis choice. However, this is not routinely done and would change workflow and significantly impact laboratory resources. The use of ciprofloxacin in combination with trimethoprim/sulfamethoxazole is not usually effective since fluoroquinolone resistant *E.coli* are often resistant to TMP-SMX (Al-Busaidi I. Infect Control Hosp Epidemiol. 2015 May;36(5):614-6).

^g We have recommended vancomycin instead of clindamycin to improve Gram-positive coverage and minimize the adverse effects from clindamycin. The ASHP recommends aminoglycoside alone with or without clindamycin. The American Urological Association recommends aminoglycoside and clindamycin in these patients but there is minimal evidence for such clindamycin use.

^h The role for azithromycin 500mg in addition to standard prophylaxis for nonelective caesarean section is supported by a recent multicenter RCT (Tita N Engl J Med 2016;375:1231-41). There was reduction in endometritis and wound infections compared to standard prophylaxis (6% vs 12% placebo; OR 0.51; 95% CI 0.38-0.68; $p < 0.001$). Before widely adopting this practice, baseline assessment of postoperative endometritis and wound infection rates should be performed to assess the need for azithromycin and to compare to post-implementation rates.

ⁱ The ASHP recommends aminoglycoside and clindamycin. There is minimal evidence for this regimen, and we recommend vancomycin instead of clindamycin to improve Gram-positive coverage and minimize the adverse effects of clindamycin.



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