Rationale for an Initiative to Reduce the Rates of Surgical Site Infections (SSI)

It is estimated that surgical site infections complicate the course of over 15% of patients undergoing operative interventions\(^1\). SSI represent the most common type of adverse event in hospitalized patients and have marked negative effects on mortality, readmission rates, length of stay, and costs\(^2\). There is strong evidence to support the implementation of several practices geared toward reducing the rate of SSI in patients undergoing general surgical procedures. Given the relative effectiveness of many of the interventions described below and the opportunities that exist to improve practice, it is now estimated that as many as half of all SSI’s might be preventable.

The primary objective of this document is to review the evidence and rationale behind these practices and provide recommendations for implementation in the University of Toronto, Division of General Surgery as part of the Best Practice in General Surgery.

1. Antimicrobial Prophylaxis

Recommendation

- Antibiotics should be given within one hour prior to incision (infusion of vancomycin should be started more than 1 hour prior to incision because it requires infusion over 60 minutes)
- For operative procedures >3 hours, antibiotics should be re-dosed (see Table)
- Antibiotics should not be given postoperatively

Prophylaxis of surgical site infections requires that bactericidal tissue concentrations of antimicrobials be present in the wound at the time of incision. To achieve this objective, antimicrobials directed against the most common contaminating organisms must be administered within an hour prior to incision\(^3,4\). Administration within this time interval results in the lowest rates of SSI. To minimize antimicrobial selection pressures, agent(s) with the narrowest antimicrobial spectrum should be used.
Preferred regimens include:

<table>
<thead>
<tr>
<th>Indication</th>
<th>Regimen (no (\beta)-lactam allergy)</th>
<th>Regimen ((\beta)-lactam allergy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastroduodenal/Eosophageal (includes bariatric surgery)</td>
<td>cefazolin*</td>
<td>vancomycin &amp; gentamicin</td>
</tr>
<tr>
<td></td>
<td>Dose: 2 g IV</td>
<td>Dose: vancomycin: 1 g IV gentamicin: 1.5-2 mg/kg IV</td>
</tr>
<tr>
<td>Biliary/Pancreas/Liver**</td>
<td>cefazolin*</td>
<td>vancomycin &amp; gentamicin</td>
</tr>
<tr>
<td></td>
<td>Dose: 2 g IV</td>
<td>Dose: vancomycin: 1 g IV gentamicin: 1.5-2 mg/kg IV</td>
</tr>
<tr>
<td>Low Risk Laparoscopic Cholecystectomy (i.e. no jaundice, age&lt;70 yrs, non-diabetic, no acute inflammation)</td>
<td>No prophylaxis</td>
<td></td>
</tr>
<tr>
<td>Breast/Hernia/Thyroid/Parathyroid</td>
<td>cefazolin*</td>
<td>vancomycin</td>
</tr>
<tr>
<td></td>
<td>Dose: 2 g IV</td>
<td>Dose: vancomycin: 1 g IV</td>
</tr>
<tr>
<td>Colon, Rectum, Small Bowel and Non-Perforated Appendicitis**</td>
<td>cefazolin* &amp; metronidazole</td>
<td>metronidazole &amp; gentamicin</td>
</tr>
<tr>
<td></td>
<td>Dose: metronidazole: 500 mg IV cefazolin*: 2 g IV gentamicin: 1.5-2 mg/kg IV</td>
<td>Dose: metronidazole: 500 mg IV gentamicin: 1.5-2 mg/kg IV</td>
</tr>
<tr>
<td>Low Risk Anorectal Procedures (i.e. hemorrhoidectomy, fistulotomy and sphincterotomy for fissure)</td>
<td>No prophylaxis</td>
<td></td>
</tr>
</tbody>
</table>

* For patients with known colonization with MRSA, vancomycin should be substituted for cefazolin

** Patients who have been on antibiotics preoperatively (e.g. Crohn’s patients) or have had instrumentation of their biliary tree should also receive gentamicin

Patients with \(\beta\)-Lactum Allergy

Vancomycin should be prescribed instead of a cephalosporin to patients with a significant allergy to \(\beta\)-lactam antibiotics. A significant allergy is defined as a prior allergic reaction (or positive skin testing) to penicillin or other \(\beta\)-lactam with resultant hospitalization or anaphylaxis. Vancomycin should be given as 1 gm IV administered over 60 minutes to avoid red man syndrome, with redosing q12h.

MRSA Colonized Patients

\(\beta\)-lactam antibiotics (e.g. cefazolin) are ineffective for prophylaxis against MRSA SSI. Vancomycin should be administered alone (e.g. in place of cefazolin) or in combination with other antibiotics active against other potential pathogens. Consideration should be given for pre-operative eradication of MRSA using oral agents and nasal mupirocin, particularly if
insertion of a prosthesis is considered. Eradication should be done in conjunction with hospital infection control practitioners or infectious disease consultants.

**Pediatric Dosing**

The preoperative dosing regimens below should be used for pediatric patients (up to age 15 years):

- Cefazolin 30mg/kg IV (max dose 2gm)
- Gentamicin 1.5mg/kg (max 120mg)
- Metronidazole 10mg/kg (max 500mg),
- Clindamycin 15mg/kg (max 600mg)
- Vancomycin 15mg/kg (Max 1g)

**Consideration of Extending the Spectrum of Gram Negative Coverage**

Patients with recent (30 d) prior exposure to antimicrobials might require a broader spectrum of gram negative coverage due to antimicrobial selection pressures. In this case, the addition of gentamicin should be considered. As an example, prior biliary instrumentation or antimicrobial exposure require gentamicin (or ciprofloxacin, to lower the risk of nephrotoxicity in the presence of obstructive jaundice) in addition to cefazolin. Similarly, patients with inflammatory bowel disease with recent antimicrobial exposure should receive gentamicin in addition to cefazolin and metronidazole.

**Intraoperative Antimicrobial Re-Administration Guidelines**

Redosing of antimicrobials for prolonged procedures is necessary to maintain adequate tissue concentrations when bacterial contamination occurs. Thus, additional intraoperative doses are recommended at intervals approximating two times the half-life of the antibiotic\(^5,6\).

For patients receiving cefazolin, they should be redosed with 1 g not 2 g.

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>Recommended Dosing Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefazolin 1 g IV</td>
<td>q3h</td>
</tr>
<tr>
<td>Gentamicin dosed at 2mg/kg</td>
<td>q12h</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>q8h</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>q12h</td>
</tr>
</tbody>
</table>

There is no evidence to suggest that postoperative antimicrobials are necessary and the continuation of prophylaxis until all catheters and drains have been removed is not appropriate.
Similarly there is evidence to suggest that postoperative antimicrobials are unnecessary even in the case of significant contamination at the time of the elective procedure.

For effective implementation, it is generally believed that protocol development requires a multidisciplinary team with a physician champion. At a minimum, this team should include representatives from pharmacy, nursing, anaesthesia, surgery, and infection control practitioners. Logistics for the assurance of timely administration of antimicrobials often requires that the agents are administered in the operating room with assurances at the time of the surgical pause or time-out. Clear delineation of roles and responsibilities for both the administration of antimicrobials and the associated documentation must be specified in the protocol. A mechanism must be put in place for routine auditing of compliance with timely feedback to the health care team.

2. Perioperative Normothermia

Recommendation

- Patients undergoing surgery where the abdominal cavity is entered should have active measures undertaken to maintain core temperature between 36.0 and 38.0°C.

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 threefold the incidence of surgical site infections after colon resection.

Mild perioperative hypothermia has also been causally linked to numerous complications including increased blood loss, adverse cardiac events, prolonged post-anaesthetic recovery and hospitalization.

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.

Resources including warming blankets, head covers, 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.

3. Preoperative Hair Removal

**Recommendation**

- Hair removal should not be performed for the purposes of SSI prevention. If hair removal is required, clipping should be used rather than shaving.

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 rates. 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.

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.

4. Choice of Skin Preparation

**Recommendation**

- Patients undergoing general surgical procedures should be prepped with chlorhexidine gluconate (2% chlorhexidine gluconate and 70% isopropyl alcohol)
- Prevent pooling of chlorhexidine gluconate on drapes and patient, and allow the antiseptic solution time to dry completely (~ 3 minutes)
This recommendation is based on a 2010 meta-analysis of 6 studies containing 5,031 patients undergoing clean-contaminated surgery (including general and gynaecological surgery) to determine whether chlorhexidine alcohol or povidone-iodine reduced SSIs. Chlorhexidine alcohol reduced postoperative SSI rates 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-iodine\textsuperscript{13}.

In addition, a recent large, multi-centre trial which included 849 patients who under went 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 clean-contaminated surgery\textsuperscript{14}.

Although these recent studies have demonstrated a 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 fire\textsuperscript{14}, this risk is due to using large 26ml applications which therefore take longer to dry, increase the risk of pooling in drapes and soaking in hair. A small amount of chlorhexidine/70% alcohol is safe as long as used appropriately (adequate drying time, avoidance of pooling and soaking of hair)\textsuperscript{15}. It is recommended that an educational program be implemented to ensure safe application of chlorhexidine/70% alcohol before its implementation.

Another concern commonly raised with chlorhexidine alcohol is cost. In 2010, a systematic review of 9 RCTs with 3,614 patients looked at the use of chlorhexidine alcohol compared with iodine. The cost-benefit model baseline scenario showed that switching from iodine to chlorhexidine resulted in a net cost savings of $16-$26 per surgical case due to the decrease in SSIs\textsuperscript{16}.

Lastly, a Cochrane Review which included 6 trials and 10,007 participants who were randomized to 4% chlorhexidine gluconate or placebo showed no clear evidence of benefit for preoperative showering or bathing with chlorhexidine over other wash products\textsuperscript{17}.

**SSI Prevention Measures not Covered by these Guidelines for Standardization**

1. Perioperative strict glycemic control
2. Intraoperative fluid management
3. Perioperative hyperoxia
There is accruing evidence that perioperative strict glycemic control and intraoperative fluid management might reduce rates of SSI. However, the available data in patients undergoing general surgical procedures is insufficient to support an argument for standardization across institutions.

There is increasing evidence that hyperoxia with FIO₂ does not reduce the risk of SSI and therefore is no longer recommended in this guideline.

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