Infection of incised tissue is an all too common yet potentially avoidable complication of any surgical procedure. “Surgical site infection” (SSI) is the preferred term, encompassing incisional (superficial or deep) and organ infections.

Health care-associated infection (HAI) is a major concern for the NHS, affecting one in 10 patients admitted to hospital. The associated costs are estimated at £1bn each year and SSIs comprise 9 to 12 per cent of all HAIs. The issue of reducing HAIs is a key government strategy and is highlighted in several documents published over the past few years (see Panel 1, p744). SSIs are associated with substantial morbidity and mortality, longer hospital stays and increased costs.

During an operation, some bacterial contamination of the operative site is inevitable, either from the patient or from the environment. The use of antibiotics is, therefore, often an essential component of the care of patients undergoing surgery. Surgical antibacterial prophylaxis (SAP) refers to the administration of a pre-operative (and occasionally an intra-operative) antibiotic to reduce the risk of an SSI developing by inhibiting growth of contaminating bacteria. However, this is only part of a strategy to reduce the risk of SSIs and is no substitute for good surgical technique. The US Centres for Disease Control and Prevention have published detailed recommendations for preventing SSIs. These include pre-, intra- and post-operative management strategies (eg, recommendations for pre-operative antisepic showering, patient skin preparation and operating room environment) as well as antibacterial prophylaxis and SSI surveillance.

Development of surgical infections

Whether or not an infection follows an incision depends on the ability of the body’s, or externally provided defence mechanisms, to destroy micro-organisms. Infections can develop when endogenous flora (eg, bacteria on the skin) translocate to a normally sterile site. An infection can also develop if the sterile peritoneal cavity is contaminated by spillage from the gastrointestinal tract. Seeding of the operative site from a distant site of infection can also occur, especially in patients with a prosthesis or implant. Surgical instruments, the surgical team and the theatre environment are exogenous sources of bacte-rial contamination. Infection is further complicated by factors such as the increased prevalence of multi-resistant micro-organisms such as methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant enterococci (VRE) in hospitals.

All patients undergoing a surgical procedure will be placed at some risk of infection. Risk factors include:

- The number and virulence of contaminating micro-organisms
- Operative and environmental factors (eg, the surgeon’s skill and theatre cleanliness)
- The nature of the operation (eg, classification, anatomical site, duration, need for implants and degree of blood loss)
- Patient circumstances (eg, age, smoking, obesity, malnutrition and immunosuppres-sant therapy)
- Concomitant diseases (eg, diabetes mellitus, renal or hepatic impairment and remote infection)
- Local factors (eg, presence of wound drains, hair removal or previous irradiation of site)

Classification of operation

There is a generally accepted classification for operations devised by the National Academy of Sciences National Research Council almost four decades ago. This classification operates according to the degree of intra-operative microbial contamination and infection. According to this classification, operations can be “clean”, “clean-contaminated”, “contaminated” or “dirty-infected”.

Clean operations include elective surgery with or without implants. The operative wound is not infected and is closed. There is no breach of aseptic technique and the respiratory, alimentary, genital and urinary tracts are not penetrated. Clean-contaminated operations include procedures where the respiratory, alimentary, genital or urinary tract is penetrated but there is minimal spillage or only a minor break in aseptic technique (eg, operations involving the biliary tract). Contaminated operations comprise open, fresh, accidental wounds. There may be visible contamination of the wound, non-purulent acute inflammation or major spillage from a hollow viscus (eg, the gastrointestinal tract). These operations usually involve a major break in aseptic technique. Dirty-infected operations are defined as procedures where there is an existing clinical infection (eg, an abscess) present at the surgical site before the operation or pus present in an injury that is usually more than four hours old.

Generally, clean procedures do not require antibacterial prophylaxis unless a prosthetic implant is involved. However, evidence of post-operative infections from other clean procedures is under-reported and antibacterial prophylaxis is advisable for some procedures (eg, breast surgery). SAP is generally required for most clean-contaminated procedures. Contaminated or dirty-infected wounds require “treatment” courses of antibiotics, not prophylaxis.

Goals of antibacterial prophylaxis

Prophylactic antibiotics are recommended when, in the absence of a prophylactic agent, there is a high risk of post-operative infection or when the risk of infection is low but the consequence is serious (ie, high morbidity and mortality). Knowledge of the likely contaminating flora is useful to inform this decision. The goals of antibacterial prophylaxis are:

- To provide optimal antibacterial prophylaxis by targeting suspected micro-organisms (with little risk of adverse effects) and minimising the development of antibiotic resistance and Clostridium difficile infection
- To reduce the incidence of post-operative SSIs
- To reduce morbidity associated with SSIs

Identify knowledge gaps

1. When is peri-operative antibacterial prophylaxis appropriate?
2. What national guidance is currently available in relation to peri-operative antibacterial prophylaxis?
3. Which antibiotics are commonly used to prevent surgical site infections?

Before reading on, think about how this article may help you to do your job better. The Royal Pharmaceutical Society’s areas of competence for pharmacists are listed in “Plan and record”, (available at: www.rpsgb.org/education). This article relates to “clinical pharmacy” (see appendix 4 of “Plan and record”).

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In the fourth article of a series on peri-operative drug therapy, Mohamed H. Rahman and James Anson discuss the prevention of surgical site infections.
The need for antibacterial prophylaxis should be determined by considering the risk and consequence of developing an SSI, the comparative efficacy and adverse effect profile of the antibiotic, patient drug allergies and local hospital resistance patterns. Deviation from usual guidelines may be necessary in some situations (eg, MRSA outbreak).

Timing of initial doses A bactericidal tissue concentration must be achieved and maintained from the point of the first incision to at least a few hours following wound closure. A single dose of antibiotic should be administered within 30 minutes to one hour before incision. Additional doses can be given if surgery is delayed.

SSIs are more likely when the prophylactic dose is administered too soon before incision — one study showed that giving a dose two to 24 hours pre-operatively resulted in a 3.8 per cent infection rate. Risk is also increased if the dose is given too late after an incision. The study also showed that rates of post-operative SSI were 1.4 per cent when the antibiotic was given within three hours and 3.3 per cent when the dose was given more than three hours after incision. However, when the dose was given zero to two hours before surgery, the infection rate was only 0.6 per cent.

In patients already on chronic antimicrobial therapy (eg, for prophylaxis of urinary tract infections), surgical prophylaxis may be unnecessary if the antibiotics being taken also cover likely surgical site pathogens. However, the timing of dosing can require adjustment to maximise the efficacy of the antibiotic.

Dose and route of administration Usually, treatment doses are used for prophylaxis but these should be governed by the patient’s body weight, especially if the patient is obese. Intravenous administration is preferred because it produces a more reliable and predictable serum and tissue concentration than intramuscular administration. Oral intraluminal antibiotics (not significantly absorbed into the systemic circulation) are occasionally used in preparing patients for colonic surgery. Oral antibiotics are generally not recommended in non-colonic surgery because of unreliable absorption and poor bioavailability.

Safety of antibiotic The antibiotic used should have minimal adverse effects. Particular attention should be paid to previous history of allergy to antibiotics to prevent a fatal allergic response. Unfortunately, idiosyncratic reactions are difficult to predict. In addition, use of antibiotics without the advice of a microbiologist may increase the prevalence of resistant micro-organisms (eg, VRE).

Single dose versus multidose therapy Many studies comparing peri-operative single dose with multiple dose prophylaxis have shown that additional doses confer no benefits. However, it may be sensible in some situations (eg, major blood loss or if surgery is unexpectedly prolonged) to administer repeated doses of the antibiotic, to ensure adequate tissue concentration throughout the procedure, especially if the antibiotic has a short half-life.

Cost-effectiveness The SIGN guidelines give guidance about calculating the cost of preventing an SSI. This can be evaluated using two key parameters: the number of patients that must receive prophylaxis in order to prevent one wound infection and the cost of prophylaxis. This cost can be compared with the cost of treating an SSI and its complications. However, the decision to provide antibiotic prophylaxis should not rely on cost alone.

Duration of prophylaxis Most published evidence demonstrates that antibiotic prophylaxis beyond wound closure is unnecessary. There is little evidence to support the practice of administering antibiotics until all drains are removed. Continuing the antibiotic does not necessarily reduce the infection rate. Moreover, it can encourage proliferation of resistant micro-organisms and subject patients to increased antibiotic-associated morbidity. Prolonged prophylaxis using antibiotics is also unnecessarily expensive. For the majority of procedures, prophylaxis does not need to exceed 24 hours (usually resulting from a single dose). Complicated, contaminated or dirty procedures may require prolonged therapy.

There are some instances where antibiotics are continued long-term. For example, post-splenectomy, prophylactic oral phenoxyl-
methylpenicillin is prescribed to reduce risk of later bacteraemia but not specifically to reduce SSI.

**Considering the type of surgery**

General guidance can be given for antibiotic prophylaxis in various surgical specialties. This section focuses on gastrointestinal and orthopaedic surgery considerations because these are the types of surgery that pharmacists are most likely to encounter.

**Upper gastrointestinal surgery**

The stomach is an efficient obstacle to bacterial colonisation, partly due to its acidic content. Treatment with agents that increase gastric pH (eg, proton pump inhibitors) can increase the concentration of gastric micro-organisms and hence the post-operative infection rate. The ASHP reports that the most common organisms cultured from SSIs after upper gastrointestinal surgery include *Clostridium difficile* 

E. coli*, *Proteus spp, *Klebsiella spp, *Staphylococci, *Streptococci, *Enterococci and occasionally *Bacteroides spp*. It recommends antimicrobial prophylaxis using first or second generation cephalosporins. In the UK, older cephalo-spors (eg, cefadine) have been replaced by second generation cephalosporins (eg, cefuroxime) given with metronidazole.

**Biliary tract surgery**

The biliary tract is usually sterile so is associated with a relatively low risk of infection. However, the presence of bacteria in the bile at the time of surgery (eg, due to biliary obstruction) increases risk. The micro-organisms most commonly associated with infection following biliary tract surgery (eg, cholecystectomy) include facultative anaerobic bacteria such as *E. coli*, *Klebsiella spp* and enterococci. Less frequently, *streptococci*, *staphylococci* or anaerobes (mainly *Clostridium spp*) are isolated.

A meta-analysis of 42 RCTs for biliary tract surgery showed that antibiotic prophylaxis was significantly more effective (the infection rate was 15 per cent in the control group versus 6 per cent where SAP was practised). In the UK, cefuroxime and metronidazole are commonly used for open biliary surgery. SAP has not been shown to reduce risk of SSI in otherwise healthy patients undergoing laparoscopic cholecystectomy.

**Appendectomy**

Appendicitis can be uncomplicated (acute inflammation of appendix) or complicated. The latter involves perforation or gangrene and can include peritonitis or abscess formation. The most common infecting micro-organisms are anaerobic (mainly *Bacteroides fragilis*) or aerobic gram-negative bacteria (mainly *E. coli*). Aerobic and anaerobic streptococci, *staphylococci*, *enterococci* and *Pseudomonas aeruginosa* have been reported occasionally.

SAP is generally recommended for uncomplicated appendicitis (despite the fact that intrinsic risk of infection is low) because the pre-operative status of the patient’s appendix is, typically, unknown. A systematic review of 44 studies showed SAP to be superior to placebo in preventing SSIs. The recommended regimen is a cephalosporin with anaerobic and aerobic activity (eg, cefoxitin) and intravenous administration of an antibiotic. In the US, oral intraluminal antibiotic therapy (eg, neomycin) is also given. A meta-analysis showed that adding an oral antibiotic was more effective than intravenous SAP alone. SAP is vital because SSI following colorectal surgery is associated with high morbidity (eg, abscess formation and septicaemia).

**Lower gastrointestinal surgery**

Colorectal surgery is associated with a high risk of surgical infection due to the high density of endogenous micro-organisms in the colon and rectum. Faecal contamination increases risk significantly so patients who are to undergo colorectal surgery usually receive mechanical bowel preparation to reduce faecal load (eg, an enema the day before the operation), before receiving a routine course of an antibiotic. In the US, oral intraluminal antibiotic therapy (eg, neomycin) is also given. A meta-analysis showed that adding an oral antibiotic was more effective than intravenous SAP alone. SAP is vital because SSI following colorectal surgery is associated with high morbidity (eg, abscess formation and sepsicaemia).

Common pathogens include *Escherichia coli*, *Streptococcus spp* and *Bacteroides spp*. A systematic review of 147 RCTs in colorectal surgery showed that SAP reduced SSIs. A first or second generation cephalosporin and metronidazole would cover the typical spectrum of gut bacteria. If *cefotaxin* is used, metronidazole is not required.

**Orthopaedic surgery**

Generally, routine, short clean orthopaedic surgery without insertion of an implant (eg, joint arthroscopy), does not warrant antibacterial prophylaxis although one or two peri-operative doses of antibiotic are routinely administered. SAP is also routine practice following non-hip surgery involving internal fixation devices, such as plates. Although the evidence for benefits of antibacterial prophylaxis in such cases is not strong, it is used because of the associated morbidity and cost if an infection were to develop.

An infection in patients following an orthopaedic implant can necessitate the removal of the implant and prolong a hospital stay. The presence of a prosthetic device reduces the number of bacteria needed to cause an SSI. Therefore, SAP is routine practice following total hip replacement, knee replacement and insertion of prosthetic devices. Antimicrobial prophylaxis is also extensively used in cases of open compound fractures, which can involve heavy microbial contamination. In addition, a systematic review of 21 RCTs showed that SAP is effective for closed fractures.

Antibiotics should be administered parenterally soon after injury. Debridement, excision of dead tissue, irrigation with an antiseptic and wound closure are also critical steps. Micro-organisms that make up the skin flora are the most frequent cause of SSIs in orthopaedic surgery. *S. epidermidis*, *S. aureus*, gram-negative bacilli and anaerobes are common pathogens.

### References


### Further reading