

Peri-operative antibacterial prophylaxis

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

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 antiseptic showering, patient skin preparation and operating room environment) as well as antibacterial prophylaxis and SSI surveillance.¹

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:

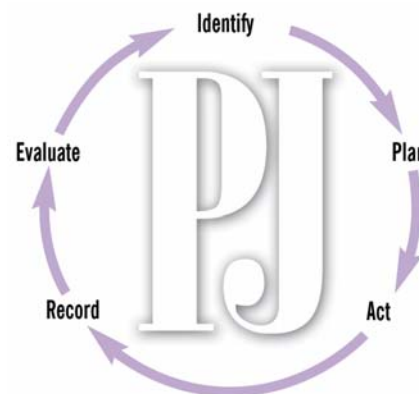
- The number and virulence of contaminating micro-organisms
- Operative and environmental factors (eg, the surgeon's skill and theatre cleanliness)
- The nature of the operation (eg, classification, anatomical site, duration, need for implants and degree of blood loss)
- Patient circumstances (eg, age, smoking, obesity, malnutrition and immunosuppressant 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 categorises operations 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 or inflamed 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



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").

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

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- To reduce mortality as a consequence of an SSI developing into a systemic illness
- To avoid prolonged hospital stays due to infection and related complications (eg, pressure sores, depression etc)

Principles of prophylactic antibiotic use

Randomised controlled trials (RCTs) have shown that prophylactic antibiotics are effective in preventing SSIs for some procedures. Considerations include the appropriate choice of antibiotic and the timing of doses.

Appropriate choice of antibiotic Eradication of every possible pathogen is not essential and evidence of efficacy from RCTs should be used to determine the most appropriate antibiotic regimen (optimal efficacy, with minimal adverse effects) that will prevent proliferation of anticipated micro-organisms for named surgical procedures.

Numerous studies have assessed a range of antibiotics (singly and in combination) for suitability as prophylactic agents in patients undergoing surgery. However, there is no general consensus in the UK regarding choice, which is currently dictated by local formulary guidelines. The Scottish Intercollegiate Guidelines Network (SIGN) gives general, evidence-based guidance on the appropriateness of SAP for a range of procedures² but does not give guidance on choice of antibiotic. SIGN categorises its recommendation for SAP under the following four main categories:

- Highly recommended (where prophylaxis explicitly reduces major morbidity and cost, for example, in knee joint replacement or colorectal surgery)
- Recommended (where prophylaxis reduces short-term morbidity but there are no RCTs to prove reduction in overall morbidity or mortality — this applies to most general surgical procedures)
- Recommended, but local policy makers may identify exceptions (where prophylaxis may not reduce hospital costs and unnecessarily increases antibiotic use, especially in low-risk patients, for example, in some obstetric and gynaecological procedures)
- Not recommended (where prophylaxis is not proven to be clinically effective, for example, in laparoscopic cholecystectomy and tonsillectomy)

The American Society of Health-System Pharmacists (ASHP) has issued general guidance as well as recommendations for antibiotic choice for a wide range of surgical procedures.³ Generally, cephalosporins are used in clean and clean-contaminated procedures because of their broad spectrum activity against gram positive and gram negative bacteria. Cephalosporins also have a good safety profile and are reasonably priced. In the UK, cefuroxime (with metronidazole for anaerobic cover) is commonly used.

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.⁴ 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.⁵ However, it may be sensible in some situa-

Panel 1: Key documents relevant to health care associated infections

- The NHS plan (www.doh.gov.uk)
- Pharmacy in the future — implementing the NHS plan (www.doh.gov.uk)
- Winning ways — working together to reduce health care associated infection in England (www.doh.gov.uk)
- Getting ahead of the curve — a strategy for combating infectious diseases (www.doh.gov.uk)
- The management and control of hospital acquired infection in acute NHS trusts in England (www.nao.gov.uk/publications/nao_reports/9900230.pdf)
- UK antimicrobial resistance strategy and action plan (www.doh.gov.uk)
- The path of least resistance (www.doh.gov.uk)
- Surveillance of SSI in English hospitals (1997–2001) — a national surveillance and quality improvement programme: nosocomial infection national surveillance service (www.hpa.org.uk/infections/publications/nin/ns/NINSS-SSI2000.pdf)

tions (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 phenoxy-

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 coliforms (*Escherichia coli*, *Proteus* spp, *Klebsiella* spp), staphylococci, streptococci, enterococci and occasionally *Bacteroides* spp.³ It recommends antimicrobial prophylaxis using first or second generation cephalosporins. In the UK, older cephalo-sporins (eg, cefradine) 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 facultatively anaerobic bacteria such as *E coli*, *Klebsiella* spp and enterococci.³ Less frequently, streptococci, staphylococci or anaerobes (mainly *Clostridium* spp) are isolated.

A meta-analysis of 42 RCTs for biliary tract surgery, showed that antibacterial prophylaxis reduces SSIs significantly (the infection rate was 15 per cent in the control group versus 6 per cent where SAP was practised).^{3,5} 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.⁵

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, staphylococcus, enterococcus and *Pseudomonas aeruginosa* have been reported occasionally.³

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.⁵ The recommended regimen is a cephalosporin with anaerobic and aerobic activity (eg, cefoxitin) at induction of anaesthesia. In the UK, cefuroxime and metronidazole are more commonly used.

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 routine 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.⁵ SAP is vital because SSI following colorectal surgery is associated with high morbidity (eg, abscess formation and septicemia).

Common pathogens include *Escherichia coli*, *Streptococcus* spp and *Bacteroides* spp. A systematic review of 147 RCTs in colorectal surgery showed that SAP reduced SSIs.⁵ A first or second generation cephalosporin and metronidazole would cover the typical spectrum of gut bacteria. If cefoxitin 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 hip fracture repair and 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

Action: practice points

Reading is only one way to undertake CPD and the Society will expect to see various approaches in a pharmacist's CPD portfolio.

1. Visit some of the sites listed in Panel 1,
2. Use the issues of the *Drug and Therapeutics Bulletin* referenced below as further reading.
3. Ensure that your hospital surgical unit has an approved set of guidelines for prophylaxis, based on safety, efficacy, local microbial environment and resistance patterns and pharmacoeconomic profile of antibiotic.

Evaluate

For your work to be presented as CPD, you need to evaluate your reading and any other activities.

Answer the following questions: What have you learnt? How has it added value to your practice? (Have you applied this learning or had any feedback?) What will you do now and how will this be achieved?

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 was effective for closed fractures.⁶

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

1. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for prevention of surgical site infection. *Infection Control and Hospital Epidemiology* 1999;20:247-78.
2. Antibiotic prophylaxis in surgery. A national clinical guideline. Scottish Intercollegiate Guidelines Network. 2000. Available at: www.sign.ac.uk (accessed 1 June 2004).
3. American Society of Health-System Pharmacists. Therapeutic guidelines on antimicrobial prophylaxis in surgery. *American Journal of Health-System Pharmacists* 1999;56:1839-88.
4. Classen DC, Evans RS, Pestonik SL, Horn SD, Menlove RL, Burke JP. The timing of prophylactic administration of antibiotics and the risk of surgical-wound infection. *New England Journal of Medicine* 1992;32:281-6.
5. Antibacterial prophylaxis in surgery: gastro-intestinal and biliary surgery. *Drug and Therapeutics Bulletin* 2003;41:83-6.
6. Antibacterial prophylaxis for orthopaedic surgery. *Drug and Therapeutics Bulletin* 2001;39:43-6.

Further reading

- Antibacterial prophylaxis in surgery: urogenital, obstetric and gynaecological surgery. *Drug and Therapeutics Bulletin* 2004;42:9-12.
- Antibacterial prophylaxis in surgery: arterial surgery in the abdomen, pelvis and lower limbs. *Drug and Therapeutics Bulletin* 2004;42:43-7.

Articles in this series

Previous articles in this series include:

- Medication in the peri-operative period. *PJ*, 6 March, pp287-9.
- Peri-operative care and diabetes. *PJ*, 13 March, pp323-5.
- Peri-operative medication in patients with cardiovascular disease. *PJ*, 20 March pp 352-4.

Further topics in this series will look at:

- Peri-operative venous thromboembolism
- Peri-operative pain, nausea and vomiting